

PROCEEDINGS  
OF THE  
ROYAL SOCIETY OF MEDICINE

EDITED BY  
JOHN NACHBAR, M.A., M.D.  
UNDER THE DIRECTION OF  
THE EDITORIAL COMMITTEE

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VOLUME THE SIXTH

SESSION 1912-13

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PART III.

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| OTOLOGICAL SECTION                        | PATHOLOGICAL SECTION     |
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OF THE  
ROYAL SOCIETY OF MEDICINE

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COMPRISING THE REPORT OF THE PROCEEDINGS FOR THE  
SESSION 1912-13

ODONTOLOGICAL SECTION



LONDON  
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1913

## Odontological Section.

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The Council think it right to state that the Society does not hold itself in any way responsible for the statements made or the views put forward in the various papers.

## Odontological Section.

October 28, 1912.

Mr. P. SIDNEY SPOKES, President of the Section, in the Chair.

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### PRESIDENTIAL ADDRESS.

GENTLEMEN,—My first words must be used in an attempt to express, to some extent, my appreciation of the honour you have conferred in appointing me to preside over our meetings and deliberations for the ensuing year. Various reasons have perhaps influenced the selection of former Presidents. I cannot in the present instance claim to have inspired the most weighty of these, but must content myself by recalling the fact that I have been a member for a quarter of a century. I ask you to believe that such an one may still be modest and humble enough to doubt his fitness for the post, but at the same time be possessed by the hope and intention to do his best to fulfil the duties of the office. With these few words of appreciation inadequately expressed, I turn from the personal aspect and must endeavour to comply with the old-established custom of presenting some remarks for your consideration upon subjects more interesting and appropriate for our meeting. And here we at once remember, that however much one may have been concerned with what may be called the "politics" of our profession, these are better dealt with by another body, and that here, in the serener atmosphere of the Odontological Section of the Royal Society of Medicine, more interesting (shall we say more useful?) problems confront us. The public health has no doubt its political and economic aspects, but we may restrict our view for the present moment to the more limited field of oral hygiene.

Members of this Section have done much in forming professional opinion upon the subjects of prevention and of treatment of dental disease; and, to focus the matter still further, the condition of

children's mouths has probably received a relatively larger amount of consideration in recent years than other dental subjects. Much remains to be done in the way of arranging diet and the inculcation of personal habits in order to secure prophylaxis, but what has already been done in the way of restoration of the function of mastication in the case of children must be considered valuable work. This is the era of "dental clinics." One hears a good deal of the institution of these in other countries, but probably the first were instituted in our own. As far back as 1886 the Anerley Board of Guardians and certain benevolent institutions seem to have done something for the teeth of the children under their care. But it was in the year 1892 that the system became established, and it is right that the credit should be given to the Central London Poor-Law School authorities for appointing a dental surgeon and providing a fully equipped "dental clinic." The example was soon followed by the various Metropolitan Boards of Guardians with the sanction of the Local Government Board. I mention this more especially because only recently the author of a paper has post-dated by ten years the institution of "dental clinics" in this country. One must hope that the good work now being done for children in many parts of the country may be extended.

Dr. Harry Campbell, in his excellent "Observations on Mastication," quotes van Someren to the effect that if the habit of masticating efficiently is once acquired, the food is not swallowed before it is converted into the liquid state, the swallowing of unmasterated lumps being effectually prevented by a pharyngeal reflex. Even if the fashionable modern diet leaves insufficient work for the teeth, the movement of the jaws as seen in mastication seems of more importance than many people realize. As Dr. Campbell points out, mastication increases the amount of alkaline saliva passing into the stomach, and this not only prolongs the period of starch digestion within this organ, but by its influence upon the reaction of the gastric contents influences all the digestive processes taking place there. Mastication influences the stomach reflexly, promoting the flow of gastric juice independently of the food, as shown in the experiment quoted by Dr. Campbell, in which, by the division of the œsophagus in a dog, no food could reach the stomach. It is probable that the influence of mastication on the flow of gastric juice is largely produced through the medium of psychic influences, for the more efficient the mastication the more is the sense of taste affected. Further, in his Croonian Lectures, Professor Starling showed that the activities of, at any rate, the large majority

of the organs of the body are co-ordinated among themselves by the production and circulation of chemical substances. Pawlow, of St. Petersburg, by making clever fistulous openings, obtained results which seemed to point to an extension throughout the alimentary canal of processes similar to those occurring in the mouth, and to prove that every gland in the canal is excited reflexly through the central nervous system, by the presence of the foodstuffs in different stages of digestion at the appropriate part of the lumen of the canal. Professor Starling's later investigations show that the correlation of functions in the digestive tract is independent of a central nervous reflex. In the case of the mouth, where all kinds of material—dry, fluid, pleasant and harmful—may be introduced, a rapid response of the salivary glands is necessary to provide for the speedy swallowing of the food, or to facilitate its expulsion from the mouth. A rapid reaction of the other glands of the alimentary canal does not seem to be absolutely necessary. The organism prepares its food for digestion or digests it by the formation of chemical substances, toxins or enzymes. The nervous system has been evolved for quick adaptations, not for the abolition of the chemical correlations which existed before a nervous system came into being.

In order that the various successive stages of digestion may follow in due sequence, each dependent upon the one preceding, does it not seem essential that the first (mastication and insalivation) shall be efficiently provided? The beneficial influence of mastication and insalivation may be exemplified by what has been found to happen in connexion with the treatment of certain cases of gastric ulcer. Dr. Rolleston and Dr. Oliver collected 1,000 cases; in 530 the patients received food, water, or both; in 470 nothing by the mouth for some days; 23 instances of parotitis occurred, 21 of them being in patients who had taken nothing by the mouth—i.e., mastication and insalivation had been absent. The authors came to the conclusion that the parotitis is an outcome of the dry condition of the mouth, and mouth-washes do not prevent it. Dr. Soltan Fenwick had similar cases, the parotitis coming on about the fourth day with a tendency to commence on the more dependent side—i.e., next the pillow. *Staphylococcus pyogenes aureus* was one of the most constant bacteria found, presumably by the infection of the parotid duct. The usual methods of cleansing did no good, so chewing various substances and the presence of a pebble in the mouth were tried. An india-rubber teat 2 in. long seems to be the best remedy and keeps the mouth clean and moist. This appears a justifiable



use for the "comforter," for in 300 cases treated since in this way Dr. Fenwick has had no trouble, although the patients were restricted to rectal alimentation for from ten days to seven weeks.

The most vivid piece of work presented in our Section this year is undoubtedly that of Mr. Howard Mummery,<sup>1</sup> whose communication to the Royal Society upon the innervation of dentine appears in the *Philosophical Transactions*.<sup>2</sup> I well remember that when I first attended lectures upon dental anatomy, and heard the accepted views as to the termination of the nerves of the pulp, I ventured to remark to the lecturer afterwards that it seemed necessary to believe that the dentinal tubes were the proper place for such terminations. Many members of the Section no doubt share with me the gratification of realizing that the industrious perseverance and histological skill of Mr. Mummery has proved our pre-conceived ideas to be not altogether unwarranted. The whole of his work on the formation and structure of such a difficult tissue as dentine must receive our highest praise, and one can only hope that he may turn his attention to enamel. Perhaps he will endeavour to explain to us the reason for the difference which many think may be observed in this tissue when the pulp no longer exists. Is the enamel on a living tooth animate or inanimate? This and other problems of living material which interest us will be made clearer by a study of the presidential address delivered recently at the meeting of the British Association at Dundee. In dealing with the question of the origin and nature of life, Professor Schäfer<sup>3</sup> naturally covered a very wide ground and made use of facts which may be taken to represent the latest views upon physiological knowledge. He said that it is becoming more apparent that the chemistry and physics of the living organism are the chemistry and physics of nitrogenous colloids. Living substance or protoplasm always, in fact, takes the form of a colloid solution. In this solution the colloids are associated with crystalloids (electrolytes) which are either free in the solution or attached to the molecules of the colloids. The "film" around the colloidal solution acts as an osmotic membrane for the diffusion of special kinds of material into and out of the protoplasm. Does not all this help us to understand the chemistry of calcification; how the soft mass of cells constituting the "enamel organ" can result in the formation of the hardest tissue of the human body? And does it not also remind us of the theory recently advanced

<sup>1</sup> *Proceedings*, 1912, v, pp. 166-90.

<sup>2</sup> *Phil. Trans.*, B, 1912, cii, pp. 337-49.

<sup>3</sup> *Lancet*, 1912, ii, pp. 675-85.

by the winner of the Cartwright Prize—namely, that Nasmyth's membrane, the external layer of the enamel organ, serves as a dialysing membrane to put the final polish upon the calcified enamel? With regard to the replantation, or even transplantation, of teeth which have been removed from a socket for an appreciable time, and where the blood-vessels, nerves and the periodontal membrane have suffered breach of continuity, practical experience has shown us that death of the pulp does not necessarily ensue. Professor Schäfer says that many cells of the body retain their individual life under suitable circumstances long after the rest of the body is dead. "Carrell has succeeded in substituting entire organs obtained after death from one animal for those of another of the same species, and has thereby opened up a field of surgical treatment the limit of which cannot yet be described."

If one ventures a comment upon the attempt to explain the origin of "life," it is in the expression of surprise that more distinct reference was not made to the possible influence of what is known by the term "electricity." More and more one is inclined to suspect that this manifestation of force probably enters as an ingredient into the constitution of both organic and inorganic bodies, and indeed permeates the universe. May not this attribute be considered as a possible factor in speculating upon the changes which must occur if the evolution of the animate from the inanimate has taken, or is taking, place? May not some change brought about in the "charging up" provide the "missing link"? We are probably only at the commencement of what is to be known about electricity, and it is only quite recently that our views upon the molecular condition of matter have perforce been changed by the behaviour of radium and its emanations. I have had the opportunity of seeing a photograph showing the helium rays coming off in a glass vessel at the moment when steam was condensed. The Alpha-rays are positively charged atoms of helium projected with a velocity of about 10,000 miles a second, the Beta-rays are negatively charged electrons projected with a velocity approaching that of light, while the Gamma-rays appear to be of a type of very penetrating X-rays. Marked chemical changes are produced by the emanation in many substances which time will not allow me to quote. May I, instead, refer to what is known as "wireless telegraphy." Among the many points awaiting solution, Dr. Fleming mentions the great variation of range which is noticed at certain times. What is the true explanation of the fact that, with given apparatus used over long distances, the effective range is about three times greater by night than by day, and why is it greatly

reduced at or about sunrise? All the above-mentioned manifestations might be taken into consideration when speculating upon the origin of "life," either going on at the present time or, as some think, in remote periods when the physical conditions of the earth were quite otherwise than at present obtain. For instance, in the discussion at a joint meeting of the zoology and botany sections, Professor Macallum quoted Tyndall that all matter was endowed with the potentiality of life, and pointed out that at one time the earth was a gigantic laboratory, where there had been a play of tremendous forces, notably electricity, which might have produced millions of times an organism that survived but a few hours; but by a favourable conjunction of those forces what we now call "life" might also have come into existence. Professor Moore said that the colloids, which were large aggregates of molecules, began to show the properties of dawning life, but it was needful also to have an energy transformer attached to the colloid. As soon as the colloids got under the influence of sunlight they started synthesizing organic bodies, and that process was going on now.

Before concluding my remarks upon this interesting question as to the nature of life, I should like to quote from a letter by Dr. Frank Skerrett published since the foregoing was written. He says: "We have applied evolution not only to biology but to every branch of knowledge. In chemistry, even, our elements are looked upon as survivals—stability under the existing circumstances being the determining factor—evolved from one primordial element. Why should we not apply the evolution hypothesis to energy, and look upon the different forms of energy—radiant, thermal, electrical, chemical, &c., culminating in vital energy—as higher degrees evolved from some original form of energy, and which in process of operation on resistant matter are apt to dissociate into some of their simpler components, thus accounting for the transformations of energy known to physics? The principle of the conservation of energy and equivalent energy is not endangered. It is one of the specific characteristics of chemical combination that the substance produced has entirely different properties from those of its constituents. No reason will explain it; we have to accept it as a fundamental fact. It is equally possible that combinations of different forms of energy might produce entirely different phenomena, including those of conscious life itself, as the highest and most finished product."

May not the phenomena of life be found ultimately to depend upon the accumulation and discharge of infinitely minute but co-ordinated thunderstorms—a bombardment of atoms, attracted and repelled, in

the smallest cell collection—finally terminating in a discharge to earth—the “mother earth” from which we sprang, and in which we have our ending?

But, gentlemen, I must forbear inflicting more of such speculations upon you lest we come to the untimely end of the philosopher who, star-gazing into the firmament above, fell into a ditch. Let us, then, come down from the clouds, and permit me to hope that we may have a useful year of work before us.

### Report of the Honorary Curator.

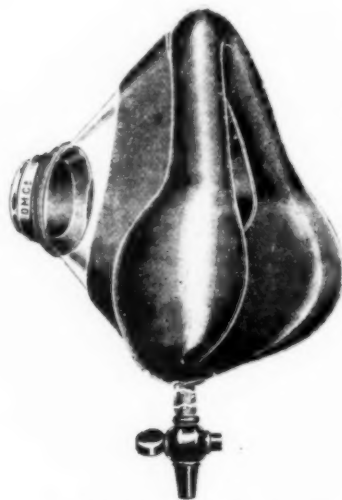
By J. F. COLYER, M.R.C.S., L.D.S.

DURING the past year sixty-two specimens have been added to the Odontological Collection in the Museum of the Royal College of Surgeons of England. Among the specimens added may be mentioned the maxillæ and mandible of a child, showing ankylosis of the temporo-mandibular articulation; a very fine skull of a lion, showing a severe injury to the anterior part of the left maxilla; a case of spindle-celled sarcoma in a dog; a Markhoor, showing extensive malignant ulceration of the left maxilla; a series of teeth from cases of periodontal disease. To the series illustrating the anatomy of the muscles of mastication five specimens have been added—namely, dissection of an Australian native, a female chimpanzee, a koodoo (*Strepsiceros kudu*), a sea-lion (*Otaria jubata*), and a capybara (*Hydrocharus capybara*). The Royal Society of Medicine has enriched the Odontological Department of the Museum with an excellent microscope and a typewriter, in addition to purchasing several specimens. It has been decided to re-number the specimens on the decimal system; the work has been commenced and it is hoped that this task will be completed during the coming year. John Hunter's specimens illustrating the anatomy and pathology of the human teeth have been remounted. It is satisfactory to note that the collection is well frequented by visitors to the Museum.

### An Improved Anæsthetic Facepiece.

By W. DE C. PRIDEAUX, L.D.S.

THE exhibitor said the ordinary anæsthetic facepiece was evidently designed to fit the facial contours when the mouth was closed. The dental surgeon required for the use of his anæsthetist a facepiece that should exactly adapt itself to the face when the mouth was propped open and the facial muscles consequently stretched. The pattern of facepiece he exhibited had ball-like swellings which fitted into the facial hollows about the mouth, making perfect adaptation quite easy and surface leakage of air or  $N_2O$  impossible.



An improved anæsthetic facepiece.

#### DISCUSSION.

The PRESIDENT (Mr. P. Sidney Spokes) said it must have occurred to many dental surgeons to adopt something of the same kind, and at times they had all pushed the rubber margin of the facepiece at the angle of the mouth, and also above the alæ of the nose. He did not know whether Mr. Prideaux was going to add rubber pieces there.

Dr. G. STEELE-PERKINS appreciated very much Dr. Prideaux's invention, because he thought it had a distinct advantage over the ordinary facepiece.

### Food and the Teeth.

By J. SIM WALLACE, M.D., L.D.S.

DR. SIM WALLACE exhibited a boy, aged nearly 12, with a perfect set of teeth, who, he said, for the last eleven years had been brought up according to the system which was going to be condemned that evening in a paper by Mr. Read. With the exception of, perhaps, two or three months during the *Daily Mail* craze the boy had always eaten white bread. Now and again, as a trial, stone-milled bread had been used, but for some reason or other it was not liked. The twelve-year-old molar below had come through, although the boy would not have attained the age of 12 for another three months.

### A Misplaced Mandibular Premolar.

By GEORGE NORTHCROFT, L.D.S.

ON February 27, 1911, Mr. T. Stordy reported a case of a misplaced second left maxillary premolar, which was found to be absorbing the roots of the first maxillary permanent molar, while the second temporary molar was still in position.

Mr. W. Rushton reported on May 8, 1912, to the British Society for the Study of Orthodontics, a case of misplaced second mandibular premolars, where these teeth were immediately behind the second temporary molars. There is no definite history of the position of the first permanent mandibular molars; they seem to have been absent altogether.

The case which I have to report contains certain features similar to both of the above, and it will be noticed that all these cases are connected with second premolars. The patient, a female, aged 24, having suffered pain in a right mandibular molar, it was extracted by a medical man; absorption of the roots of this tooth had probably taken place. Pain continued, accompanied by a discharge and a certain amount of swelling; this was at first diagnosed as due to a portion of root having been left behind, but just as the examination was ended

the extreme hardness of the supposed fragment was detected, but as it was so low down in the socket an X-ray was taken for confirmation, before further operation. This showed that the supposed fragment of tooth was a fully formed premolar. The socket was packed and the tooth removed across the mouth by a pair of upper Reeds in the usual way. Unfortunately no history could be obtained of the congenital absence or extraction of  $\bar{c} \mid$ .

The interest of the specimen lies in its indentation by the mandibular nerve on the lingual surface of the apex of the root, and that the premolar branch was given off from the lower and buccal instead of the upper and lingual surface of the main trunk, as shown by a skiagram of the tooth. It also incidentally proves that the formation of the root is not a factor in eruption.

The interest of all these cases seems to be a developmental one. How did they occur? It will be seen that my own case is similar to Mr. Rushton's, excepting the absence in his case of  $\bar{c} \mid \bar{c}$ , and mine is only unilateral.

We now know that irregularities occur as frequently in the temporary as in the permanent dentition, excepting, of course, those caused by extraction; that the periods of eruption of the temporary teeth are just as full of variation as those of the permanent set—therefore the times of the formation of the tooth-buds will follow the same course.

In Mr. Rushton's case, if at the end of the seventeenth week of intra-uterine life the *Zahnleiste* had not become thickened for the tooth, germ of  $\bar{c} \mid \bar{c}$ , but development had been arrested for a short time, it is conceivable that the tooth-bud for  $\bar{5} \mid \bar{5}$  given off at the normal time and place, thirty-three weeks, would then grow downwards and backwards, arresting the impulse of growth of  $\bar{c} \mid \bar{c}$ , which had been delayed. It is well known that first molars do not erupt sometimes until eight to nine years. The second molar-bud could still be given off at the normal time and place, four months after birth.

Mr. J. F. Colyer is reported to have explained the condition as an atavistic tendency, relating to the backward slope of developing  $\bar{5} \mid \bar{5}$  in apes; but even in apes the teeth are successional to ones immediately above them.

In my own case, if one remembers that the tooth-germ buds off from a band of tissue going right round the jaw, and that this main band continues downwards after the temporary germ has been given off, then if at thirty-three weeks the thickening of the *Zahnleiste* for the permanent bud took place backwards and downwards instead of directly



downwards, it is conceivable that the second premolar would develop under the first molar, which had reached already a higher level in the jaw, being sixteen weeks old.

It might be argued that this whole abnormal condition had arisen from very early extraction of  $\bar{e}$  and the forward migration of  $\bar{6}$  over the growing  $\bar{5}$ .

An inspection of the X-ray seems to show that  $\bar{6}$  was never in contact with  $\bar{4}$ , and that there was consequently room for  $\bar{5}$  to erupt normally had it developed in a normal position. The models have only been taken recently, but by studying the occlusion it will be seen that  $\bar{8.7}$  have travelled very much forward, even more than when the case was first seen seven months ago.

### Bread in its Relation to Dental Caries.

By THOMAS G. READ, L.D.S.

(ABSTRACT.)

THE deterioration of bread is due to the removal of the ferments contained in wheat, in order that flour may be kept for a long time without becoming rancid. The removal of the ferments, besides diminishing the nutritive value of bread, has caused it to become harmful to the teeth.

A grain of wheat consists of an envelope enclosing a hard kernel, and a softer body, which is the vital part or germ. The envelope or husk consists of three coats, which are chiefly composed of woody fibre and cellulose, with a little protein. The husk is rich in mineral matter, so placed as not to be readily assimilated by the human system, although some birds and animals, being better able to digest parts of the bran, do assimilate the mineral matter. Nature has provided wheat with these outer coverings to preserve its vitality. The kernel consists of irregularly shaped cells containing starch and protein. The cell walls are made of cellulose. The kernel is very deficient in mineral matter, a little being in the outer portion but practically none in the centre. The germ or vital part of the grain consists of the embryo or young plant; this is separated from the other part of the grain by a layer of columnar cells, in which the ferments have their origin. The germ is the most important part of the grain owing to the chemical action of the ferments



it contains. It also contains fat, protein, and mineral matter. The human system can more readily assimilate the mineral matter of the germ than that contained in the husk. Under the influence of suitable moisture and moderate warmth certain changes take place. Two ferments commence to operate; one acts on the cellulose, and the other, known as diastase, acts on the starch of the kernel, converting it into glucose. By such means the insoluble cellulose and starch are rendered soluble. The ferments of wheat, if not destroyed, act during malting, bread-making and its equivalents, mastication or digestion. The diastase converts starch into glucose in the grain, the meal, the flour, or the dough. The presence of this sugar may be demonstrated by testing. When the grain has been malted, it will be found both in the flour and in the bread; when the unimpaired ferments are present in the flour, it will not be found in the flour, but it will be found in the bread; and when the ferments have been destroyed or removed, it will be found neither in the flour nor in the bread. Some flours now have sugar added to them before being made into bread. The most reliable way to decide whether the ferments have performed their action is to test bread for acidity before and after mastication. Glucose is best formed in human food during malting, or bread-making and its equivalents. Animals fed on grain form glucose during mastication and digestion. Grain-eating birds form glucose during digestion, the grain being ground up in the gizzard. Birds swallow grain whole, and some animals bolt their food. A most important point is that the outer coverings of grain preserve the vitality of the germ. When millers destroy this by heat the nutritive value of bread is diminished and the teeth destroyed by the acid forming during eating. Meat deteriorates if kept longer than a certain time, as it becomes putrid. When wheat is ground up with the germ containing the unimpaired ferments the flour if kept a long time becomes rancid. Although this flour cannot be kept so long as most present-day flour, it makes bread that does not become stale so quickly as most of our bread does now. Formerly many consumed bread that was baked only once a week. Properly prepared week-old bread, composed of stone-made flour, is more pleasant to eat than most of our new and day-old bread.

The two methods of preparing flour from wheat are known as stone-milling and roller-milling. Stone-milling is a simple method by which all parts of the grain are cut or torn apart during passing from the centre to the periphery or skirt of the stones. The flour produced consists of fine particles of all parts of the wheat, and is obtained after grinding

by sifting it from the coarser pieces. The colour of bread produced from stone-made flour chiefly depends on the amount of fine particles of the husk in the flour. Roller-milling is a complicated method, and instead of only one kind of flour being obtained, several different grades are produced, all of which when made into bread decay the teeth during eating. In a roller mill the wheat is first crushed between a few pairs of break or fluted iron rollers. After each crushing the flour is sifted out and regarded as of low grade. Before passing to a number of pairs of reduction or smooth iron rollers to be pulverized the crushings undergo a process of siftings and air-blasts. Then certain parts are passed on and pulverized by the reduction rollers. After passing between each pair of smooth iron rollers the flour produced is sifted out; that from the first few pairs is considered to be high grade, and that from the later pairs low grade flour. Bread composed of roller-made flour consists almost entirely of starch and gluten. There are no particles of the germ or the husk in the flours produced, as the chief object of a roller miller is to obtain germless and branless flours.

Some dentists have regarded bran as an important source for the supply of lime salts for the formation of teeth. Coarse pieces of offal act as an irritant to the mucous membrane of the intestines; then when given to children the passage through the alimentary canal may be too rapid for food to be properly assimilated.

The ideal bread for general consumption, especially for children, or the loaf for the preservation of good health and sound teeth, is of a creamy-white colour and composed of stone-made flour; not a mixture of stone-made flour and strong or water-absorbing roller-made flour, so that many loaves may be produced. The ideal flour is that obtained from unwashed clean English wheat, which has been recently ground, should contain the unimpaired ferments, and consist of from 70 to 75 per cent. of the wheat ground. The about 28 per cent. to 23 per cent. of the grain removed from the flour should consist chiefly of the indigestible woody fibre of the husk and cellulose. Bread should be made with fresh brewer's yeast.

All freshly made flours are free from acid, but all breads are slightly acid and become more so when stale; the crust or outer part of the loaf being the most acid. The stale natural acid of bread does no harm to the teeth, and in the mouth it is always more or less diluted. It is the forming of nascent lactic acid that does harm, but once formed it soon loses the stronger decomposing action of its nascent state.

If a number of sound teeth be obtained and the crowns be embedded in freshly chewed breads, in a warm room, some in bread when the ferments have not performed their action, and some in bread when the ferments have performed their action, removing the teeth from the chewed breads about as frequently as the mouth is refilled and emptied during eating, wiping them, and replacing them in freshly chewed breads, it will be found that the teeth which have been embedded in chewed bread when the ferments have not performed their action will soon show signs of disintegration; whereas the teeth which have been embedded in chewed bread when the ferments have performed their action will not be affected.

Lactic acid forming during the mastication of bread while in its nascent state dissolves the lime salts of the enamel. Minute quantities of lactic acid frequently forming in the mouth during eating, and while passing through the mouth, each minute quantity, only remaining a brief period in contact with a portion of a tooth, dissolves a little of the lime salts, and thus disintegrates a speck of the enamel surface. When the frequent attacks of minute quantities of nascent lactic acid have eaten through a spot of enamel a minute speck of decay can be detected. Each fresh supply of lactic acid, while forming, is likely to decay the tooth a little more until a sufficient cavity is made for food to find a lodgment; then the attacks are more prolonged and the decay proceeds more rapidly.

When the unimpaired ferments of wheat are present in the flour the diastase of the wheat-germs converts starch into glucose during bread-making. When this bread is masticated no acid is formed during chewing, and the glucose passes unchanged into the alimentary canal. When bread contains this sugar formed during bread-making it has to remain for hours in the mouth for acid to be formed from it. Thus, when no other bread is eaten than that in which the ferments have performed their action, the chance of dental caries is almost non-existent, as far as bread is concerned, as may be seen by examining the mouths of those who eat no other bread than that composed of stone-made flour; for example, the *pot-au-feu* eating peasants of France, who have well-developed jaws and sound dentitions and eat no other bread than that composed of stone-made flour, produced from clean, unwashed French wheat containing the unimpaired ferments.

When the ferments of wheat have been impaired, destroyed, or removed during milling the flour, no glucose is formed during bread-making. When this bread is masticated lactic acid is very rapidly

formed in the mouth, as the *ptyalin* of the saliva rapidly converts starch into glucose, and from this forming sugar, bacteria in the mouth form lactic acid.

There has been a tendency to over-estimate the importance of bacteria in the causation of dental caries. Experiments have been conducted by incubating for from sixteen to one hundred and fourteen hours various dietetic substances to which had been added bacteria cultivated from carious dentine; then, according to the quantity of bacteria produced, it was suggested the tooth-decaying power of a given food might be known. Since it is forming or nascent lactic acid that disintegrates tooth tissue, it matters little what quantity of bacteria be in the mouth, unless a food be eaten from which the bacteria can form lactic acid. Acid-forming bacteria are always more or less present in the mouth; but they can only form lactic acid from certain foods; thus the presence of these foods determines whether teeth decay. Bacteria cannot be banished from the mouth, but bread that forms lactic acid during eating can.

The conversions from starch to lactic acid are only a matter of seconds in the mouth. Thus when bread in which the ferments have not performed their action is eaten, the chance of dental caries occurring is very great, even when no food lodges in the mouth. The lodgment of food around the teeth is more a sign than a cause of dental caries. The primary cause of dental caries is nascent lactic acid dissolving the lime salts of the enamel, and this above all happens without any lodgment of food. When teeth are already decayed food lodges in the cavities formed, and when teeth have fillings in them food is often inclined to rest around them. Little if any food lodges in the mouth when the dentitions are sound. When bread made from flour containing the unimpaired ferments is eaten it has to remain in the mouth for hours for any acid to be formed; therefore it does no harm while passing through the mouth. When bread made from flour not containing the ferments is eaten, lactic acid, rapidly forming, disintegrates tooth tissue without any bread resting. When bread that forms lactic acid during mastication has been eaten, the harm already done cannot be reduced by eating detergent or cleansing foods, or by washing or brushing the teeth after meals, or by rinsing the mouth with mouth-washes.

Oral detergency can never prevent dental caries while bread is eaten that during mastication forms lactic acid from forming sugar. Nascent lactic acid acts so rapidly on tooth tissue that harm is done before any

detergent or other imaginary preventive agent of dental caries can act. Since each minute quantity of lactic acid forming during eating is only a brief period in the nascent state, and although the formation of fresh supplies of lactic acid continues for some time, the stronger decomposing action starts with the first minute quantity forming; therefore to prevent dental caries occurring the first minute quantity must not be formed in the mouth.

The only method of insuring sound dentition is to avoid eating foods which form lactic acid during eating.

Sugar which has been formed previous to being introduced into the mouth remains a number of hours in the oral cavity before forming lactic acid. Since but little food lodges for hours in a healthy mouth, the risk of dental caries being caused by lactic acid forming from sugar already formed is not as great as some would have us believe; in fact, it is only a minor risk. The major risk is lactic acid forming during eating from forming sugar.

Some years ago I kept a number of loaves made from different flours to check what amount of weight was lost by age. I went away for a holiday, leaving the loaves on a shelf, and when I returned found that mice had eaten the insides of two. These were composed of stone-made flours. Those composed of roller-made flours were not touched. The mice, when they had the chance, ate the superior bread in preference to the inferior.

Having conducted various experiments I can with every confidence in the knowledge of the correctness of the facts state that stone-made flour produces the best bread for the preservation of good health and sound teeth, and that impairing, destroying, or removing the ferments of grain, besides destroying the teeth destroys life under some circumstances.

We have heard much about a cheap loaf, but what is of more importance is bread of the highest possible nutritive qualities. Much present-day bread is dear at any price, as it impairs the health and causes the teeth to decay.

## DISCUSSION.

Dr. SIM WALLACE said several points had occurred to him whilst listening to the paper, the first point being the effect of breads on the *corpus vile*. Mr. Read had put forward nothing of a practical nature to indicate why stone-milled bread was presumed to be so very excellent for the teeth, and white bread so very bad. He himself, however, had brought forward a case—the boy he had shown earlier in the evening, and he was only representative of several others by the parents of whom the nature of the bread was not considered of any importance at all. All farinaceous foods were supposed, under the system he advocated, to be somewhat dangerous, and consequently they were always followed up by some food of a detergent nature. The detergent food most commonly used in the case of the boy was an apple, but any other fruit available was generally willingly taken, the only fruit objected to being persimmons. At a meeting of the Section last year Mr. Coxon stated that it was his lot to look after three children who were fed very carefully on bread made from the finest red and white flour from which nothing was extracted; it was very carefully prepared, ground in a stone mill, and the only bread the children were allowed to have; and at the ages of 25 to 22 the teeth were decidedly worse than in the case of the parents, though the children themselves were fine specimens of healthy human beings. The child he had shown that evening was his own, and he was able to say that the parents had particularly bad teeth; he himself had a vivid recollection of the first permanent molar being extracted at about the age of 8, and by the time he had reached the age of 12 he had quite a crop of fillings. Mr. Read thought that caries was due to the nascent lactic acid formed during the act of mastication, and that the lodgment of food had very little to do with it. If Mr. Read would look into the mouth he would see that caries did not occur so much on the parts of the teeth that were subjected to mastication, such as the cusps, but that decay occurred in the crevices of the masticating surfaces, or the necks of the teeth, or between the teeth where no mastication took place, but where a good deal of food might lodge. He had noticed himself that there was more decay in the teeth of children who did not masticate their food properly than in those who did masticate their food. With regard to the theoretical part of the subject, the experiments of Martin Flack, Leonard Hill, and James Wheatley on the subject of fermentation of stone-milled bread had not been referred to in the paper, the reason probably being that they did not support the contention Mr. Read put forward.

Mr. READ said that was not the case: he had as far as possible avoided matter he had dealt with previously.

Dr. SIM WALLACE said he would be glad if Mr. Read would refer to it in his reply, and also say something about the nascent lactic acid. Where was



it formed? Was it formed in the nascent state during the metabolism of the sugar in the substance of the bacteria, or was it formed outside the substance of the bacteria? Was it the product of metabolism? Was it a fact the enamel was decalcified in advance of the bacteria? If so, then it could not be nascent lactic acid, but lactic acid that had been formed outside the enamel penetrating gradually into the enamel. He would strongly advise persons with children not to rely on stone-milled bread for preventing caries in the teeth. It was now a fairly well established principle that farinaceous food was not injurious if the teeth were cleansed afterwards by eating a detergent food, which stimulated all the self-cleansing processes of the mouth.

MR. UNDERWOOD asked whether it was possible to have fermentation without bacteria. It seemed to him that bacteria were necessary.

MR. F. J. BENNETT said most of the statements in the paper were perhaps more or less well known to the members previously. Mr. Read had divided his subject into two main points, one being the question of the general nutritive value of the bread made from roller-mill flour, and the other being its local effect upon the teeth. Most of the matter connected with the general nutritive value of bread had been gone into thoroughly by Dr. Leonard Hill, who fed mice and rats upon the two varieties of bread, and admitted that those which were fed upon the white flour lost weight and ultimately died. That, as far as it went, seemed fairly conclusive, but there was a concluding investigation of Dr. Hill which threw a totally different light upon the matter. As soon as he began to feed his rats and mice upon white bread or brown bread, or any kind of bread, with other ingredients which afforded the animals a mixed diet, the rats and mice put on weight without regard to the kind of bread taken at all. Dr. Leonard Hill was satisfied that for an animal which took a mixed diet white bread was as good as wholemeal bread. With regard to the question of dental caries, it was quite new to him to learn that lactic acid was formed in the act of mastication. Those who had conducted experiments knew that it was in the interstices of the teeth, where particles of food, bread, or starch lodged, and were allowed to remain in the moist warmth of the oral cavity, that lactic acid was formed. Again, as Dr. Sim Wallace had pointed out, if lactic acid was formed in the act of mastication, one would expect to find the cusps and all exposed portions of the crown of the tooth to be equally affected, but that was not the case. With regard to the question as to what was the exact chemical action taking place in the process of fermentation, he believed it was generally allowed to be somewhat similar to vinous fermentation; the bacteria broke up the molecule of sugar, and oxidized it into lactic acid. Recently Mr. Turner had handed him some specimens of ancient Egyptian teeth and he found they were very largely affected by caries. These specimens convinced him that any question of roller-mill flour was outside consideration, inasmuch as three thousand years ago there was no such thing as a steel mill.

Mr. W. RUSHTON said that in the face of the recently discovered cause of beri-beri the question of the preparation of food was of extreme importance. It had been found, in countries where rice was the staple food, that the taking away of the husk of the rice produced very alarming nervous symptoms, frequently ending in death. It had been discovered, however, that if an extract made from the rice polishing was administered to the sufferers they could be restored once more to health. The question of modern food preparation and preservation was an extremely important one, and in that connexion Mr. Read certainly had scored a point. But whether the other remarks in the paper were equally germane was more open to question, especially the point of the nascent lactic acid. It was well known that when nascent acid was formed it was of an extremely active nature, and eagerly combined with anything that was capable of combining with it, and therefore one might naturally feel captivated by the argument put forward; but, as some speakers had already said, the formation of lactic acid was not instantaneous, but of slow growth, and therefore the argument fell to the ground. Again, if there were anything in the argument, the teeth most used would be the teeth most attacked, but we knew it was not so. The wisdom tooth, when it was not functional for instance, was inclined to decay very rapidly; and it was thought it decayed probably because it was not cleansed as well as the other teeth, that food congregated round it, and consequently lactic acid was slowly formed, especially between the cheek and the buccal surface, and the tooth decayed quickly. But if the second molar had been extracted and the wisdom tooth became functional, the tooth very often remained sound for very many years, owing to the fact that it had a better chance of being cleansed. As the question of dental caries had been touched upon, he should much like to know whether it was to be considered that there had been any deterioration in the actual tooth fabric. A little time ago Mr. Stanley Mummery brought forward experiments which seemed to go a long way towards proving that such was the case. If it were so, was the deterioration due in any measure to heredity or to pre- or post-natal mal-development? He could not accept the theory that it was due to lactic acid or any other environment alone. A short time ago he had read in a pamphlet issued by the National Food Reform Association that the question of the standard loaf had seriously engaged the attention of Mr. John Burns, and that some announcement with regard to it would be made in Parliament this Session. This might be a matter of consolation to Mr. Read.

Mr. HOWARD MUMMERY said he could not follow Mr. Read when he appeared to think that dental pathologists considered caries to be due to the number of bacteria in the mouth irrespective of their nature or of the pabulum found in the mouth at the same time. Everyone, he believed, had understood it was due to the presence of lactic acid fermenting bacteria when carbohydrates were present in the mouth, and those were the conditions under which nascent lactic acid was formed. His son's experiments went to show



that there was a difference in the quality of the enamel, that the enamel was affected by nascent lactic acid when in a stagnant condition in different degrees, and he thought it was universally acknowledged that all caries arose from the accumulation in some form or other of carbohydrates in which fermentation from bacteria took place. If it occurred on the surface of the teeth it arose in fissures, or beneath the so-called bacterial plaques which were certainly often formed there; if between the teeth, from the accumulation of food in that situation; but in every case the *stagnation of food* containing fermentable material in the presence of suitable bacteria was the determining cause of caries.

Mr. STANLEY MUMMERY said with regard to the experiments that had been mentioned, that he had noticed that when teeth were placed in a mixture of food and incubated, an acid reaction of the medium certainly did not occur under an hour. Therefore, it was impossible to conceive how lactic acid could be formed during the process of mastication.

The PRESIDENT said that an expression occurred more than once in the paper—viz., "unwashed, clean wheat." At first sight that was a contradiction in terms, but no doubt Mr. Read could give an explanation. Another thing he would like to know was how the roller mill people got rid of the essential germ and its ferments. Did they deliberately stand at a certain pair of the rollers where the ferments could be expected to arrive and then dust them out, or were they dealt with in some other way?

Mr. READ, in reply, said Dr. Sim Wallace had accused him of producing no facts, but he thought that accusation was not justified. Eleven years ago he produced before the British Dental Association reports from two chemists of repute on the formation of acid during the mastication of bread, but judging from the discussion that evening the reports might never have been produced at all. He thought a sub-committee of the Society should be formed to go into the whole matter and make experiments, which could be carried out in the Chemical Department of the Royal Dental Hospital. In that way it would be possible to test all sorts of bread for acidity before and after mastication. He had obtained acid from masticating roller-flour bread, but no increase in acidity when stone-made flour bread was masticated.

Mr. F. J. BENNETT said the acid was there already.

Mr. READ said that both kinds of bread had carbonic acid, but he found he could produce lactic acid from one bread by mastication but not from the other. At the National Dental Hospital Mr. Hugh Candy, when told that one bread produced acid during mastication and the other did not, would not credit it at first, but was quite convinced of the fact after experiments, and furnished a report upon the subject later on. A friend, Mr. J. B. Knight, an analytical chemist to a large firm, during the tests he conducted, had a large quantity of roller-flour bread masticated and extracted an appreciable

amount of lactic acid from it. Dr. Leonard Hill, on feeding rats with standard flour not containing the ferments, found only an increase of 13 per cent. in weight, but when feeding with standard flour containing the ferments there was an increase of 45 per cent. in weight.<sup>1</sup> When Dr. Hill was testing for acid he found all the breads he used had acid before and after being chewed. He did not use for his tests any bread after the ferments had performed their action.

Mr. F. J. BENNETT said his statement had nothing to do with the local condition. When he quoted Dr. Leonard Hill it was as to the increase in body-weight under the two forms of bread, but as far as he could remember Dr. Leonard Hill had made no experiments connected with acid in the mouth.

Mr. READ said Dr. Hill's report would be found in the *British Medical Journal* of June 3, 1911, giving a number of figures with regard to increase in acidity during mastication. With regard to mastication, it did not follow that the only part of the teeth affected would be the cusps; the acid might be formed on the sides, and the lips, cheeks and tongue would press it into the teeth. If acid was formed during mastication there would be a further increase of acid from food lodging between the teeth. With regard to Mr. Underwood's remarks, he did not wish to be taken as saying that bacteria had nothing to do with the matter. What he had said in the paper was that bacteria might be there and do no harm unless they had the proper medium to convert into lactic acid. With regard to a mixed diet, it should be remembered there was a large number of children, especially in the East End, who lived on nothing but bread, and it was important from the point of view of those children that the bread should be of the highest nutritive quality. Mr. Bennett had referred to Egyptian skulls and the decay found in the teeth. It was true there were no roller mills in those days, but the ferments might have been killed by heat. As to polished rice, a certain amount of the germ came away with the husk. With reference to the quantity of bacteria mentioned by Mr. Mummery, as long as there were sufficient bacteria to make the acid that was all that was necessary. It mattered not how large the number of bacteria, they could not make lactic acid without the necessary food from which to produce it. As to the time of fermentation, Mr. Hugh Candy and Mr. John Knight both found with roller-flour bread an increase of about 40 per cent. of acid during mastication over the amount previously there—i.e., it increased about half. Recently Dr. Leonard Hill and Dr. Martin Flack, using standard bread made from flour when the ferments had been destroyed during milling, and white bread made from flour when the ferments had been removed during milling, having chewed bread for two minutes, found an increase of acidity in both the breads they used. The acid must have been nascent to have been formed. With reference to Mr. Spokes's remarks, by clean wheat was meant

<sup>1</sup> *Brit. Med. Journ.*, 1911, ii, p. 597.

wheat that had no rust or smut. The great object in washing wheat was not so much the washing as the drying, because the drying killed the ferments. Flour containing the ferments had to be used very quickly, and that was why millers and bakers did not like it. The germs were removed by the iron rollers flattening them out sufficiently to prevent them passing through the silk of the dressing machines; whereas in the stone mill all parts of the wheat are cut or torn apart, the action of the stones on the grain being very similar to filing.

## Odontological Section.

November 25, 1912.

Mr. P. SIDNEY SPOKES, President of the Section, in the Chair.

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### A Short Supplementary Note on the Nerves of the Dentine.

By J. HOWARD MUMMERY, M.R.C.S., L.D.S.

I ONLY propose to make a few remarks on the specimen under the microscope on the table, and the drawings and photographs which I have prepared to explain it. Since reading my paper in June last I have been preparing fresh sections, and was successful in procuring a very instructive preparation by the Beckwith gold chloride method. Those who have cut many sections of the pulp *in situ* know the great difficulty of obtaining sections which are exactly parallel to the nerve-bundles for any considerable distance, and this has been one of the great sources of difficulty in tracing the ultimate nerve-fibres to the main bundles of fibres in the substance of the pulp.

In the slide I am now showing the section included the termination of a nerve-bundle in the pulp spreading out into a brushlike expansion of ultimate nerve-fibrils, and the latter are traceable throughout their whole course from the nerve-bundle into the dentinal tubes. In this situation the plexus beneath the odontoblasts appears to be absent, the nerve-bundle immediately sending out fine fibrils to the dentine margin. It will be noticed, however, that most of these bend laterally before entering the dentine, and there is an indication of a marginal plexus, but none of a plexus deeper in the pulp. This specimen reminds one of the drawing shown in Professor Römer's paper, a copy of which I have placed upon the table—he shows fibres passing into the dentine, and bending round before doing so. His specimen was from the tooth of a kitten, and was stained by the *intra vitam* method, with methylene blue. The nerve-fibres he shows are detached, and their connexion with the main nerves of the pulp is not shown as in my specimen, but

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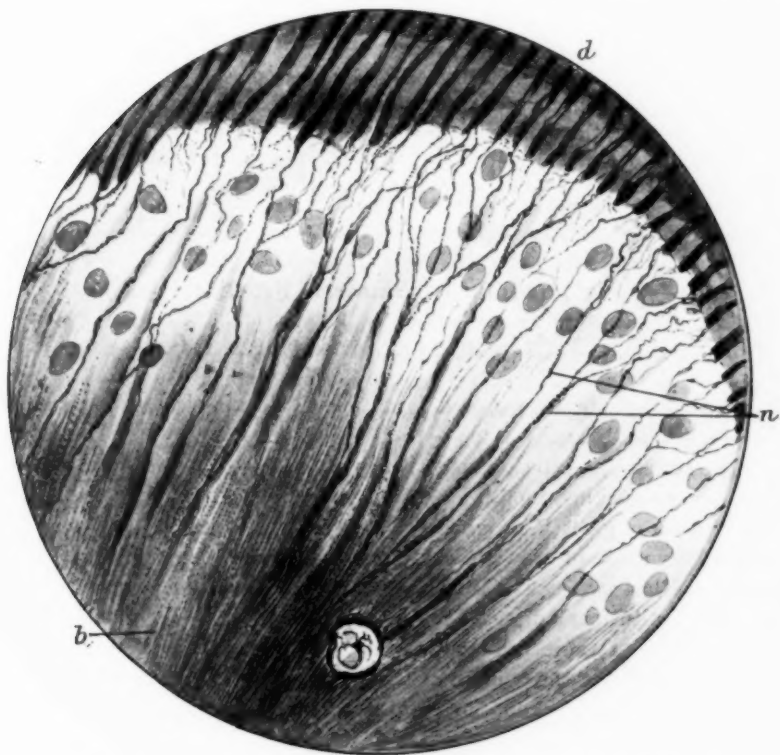
I think there can be little doubt, as I have said elsewhere, that these fibres figured by Professor Römer in the single drawing he gives in his paper are really nerve-fibres.

I had long thought that at the tip of the cornu the best demonstration of nerve-fibres would be found, as many of the large bundles of medullated fibres in the pulp traverse it to the cornu without giving off any large branches. As you will see in the microscope, the nerve-fibres emanating from this bundle are very distinct fibres, *beaded* as they all are, but probably being made up of many neurofibrils destined to divide in the substance of the dentine, are larger than those I have shown at the pulp margins elsewhere.

For comparison I will show the lantern slide of the expansion of the fibres in this situation which I used in illustration of my former papers. In this slide the fibres are not traceable to the dentine, but the brushlike expansion is in the same situation in this rather thick section as in the thin section under the microscope and photograph of which I will now show. These strands of nerve-fibres passing to the dentine appear to be much larger than those I have described as passing from the plexus to the dentine in other parts of the tooth; these strands, however, are not separate fibres, but, as a careful examination of the specimen will show, are *bundles* of fine non-medullated fibres. In longitudinal sections I have frequently seen these larger bundles at the apex of the pulp cornua, spreading out as in this specimen, but from the fact that the dentine in this spot is so frequently cut at a tangent I could not trace them with any accuracy to their destination. In this case, however, the dentine is cut in the same plane as the nerve-bundle, and the distribution from the main terminal trunk is very clearly seen.

One would imagine from an examination of this specimen, and from the brushlike termination before described in the iron and tannin preparation, that at the apex of the pulp the nerves are given off to the dentine more directly than elsewhere, and in larger bundles of neurofibrils. This can, I think, be easily understood, as more numerous and longer dentinal tubes radiate from the pulp apex than from its sides, and a larger supply would be called for—these larger bundles of neurofibrils dividing and subdividing in the dentinal tubes and their branches. At the neck of the tooth, and at the periphery of the pulp generally, they are given off in much smaller bundles, and enter into a more intricate plexus than at the apex, both beneath the odontoblasts and at the dentine margin. On the table is a preparation showing the usual arrangement at the periphery of the pulp.

As all gold specimens are very apt to fade, I thought it might be interesting to the members of the Section to see the slide while still in perfect condition. The counter-stain is weak toluidin blue to act as a nuclear stain only. The second microscopical slide under the microscope shows a bundle of fibres in the pulp accompanying a



From the cornu of the pulp of a human bicuspid, stained by Beckwith's gold chloride method. *d*, dentine; *b*, a main nerve-trunk breaking up into a brush-like expansion of neurofibrils; *n*, terminal strands of neurofibrils passing to the dentine and entering the tubules. ( $\times 800$ .)

blood-vessel stained by the same method. It will be noticed that this stain brings out the dotted axis cylinders in the main trunks very clearly—the medullary sheath, of course, not being stained. The counterstain in this case is eosin. I have shown this slide for

comparison with the other, and I think you will see very distinctly that the terminal bundle is composed of the same beaded fibres as those which compose the axis cylinders of the main nerves of the pulp.

MR. HARRY BALDWIN congratulated Mr. Mummery on his exceedingly fine work, which fully demonstrated the termination of the nerves of the pulp in the dentine. The Section was very proud of Mr. Mummery. The greatest microscopists of this country and the Continent had been engaged in similar work for many years, and yet they had always failed to do what Mr. Mummery had finally succeeded in doing. When Mr. Mummery had brought the matter before the Section on a previous occasion there had been a certain amount of discussion about the interpretation of the appearances, but he thought everyone would now admit that Mr. Mummery had removed the matter from the sphere of controversy and had absolutely demonstrated his case.

### Orthodontics in Modern Practice.

By J. H. BADCOCK, M.R.C.S., L.D.S.

THE immediate causes of deformities of the masticatory apparatus may be divided roughly into:—

- (1) Mechanical interference with growth—e.g., retained temporary teeth, thumb-sucking, mouth-breathing.
- (2) Lack of growth, as when general crowding occurs.
- (3) Perversion of growth—e.g., abnormal relation of jaws.

Now these last two causes, lack of growth and perversion of growth, are due to constitutional diseases, of which rickets may be taken as an example. Then there are certain other things which have been given as causes. One, in the opinion of Dr. Sim Wallace, is insufficient use of the jaws, the tongue and the cheeks in the act of mastication, which causes a lack of development, a lack of stimulus to growth, and a lack of proper arrangement of the teeth in normal arches. On the other side we have Mr. J. G. Turner, who tells us that in the mouths of idiots, who from their infancy have never been able to take anything more solid than pap, he very frequently finds perfect dental arches. These two views are very difficult to reconcile. That is one of the points on which I want enlightenment this evening.

The premature extraction of teeth is put forward as another cause. I came across a note in the *British Dental Journal* the other day of some interesting experimental researches which have been made



by Dr. Lansberger, of Berlin, on this subject. His object was to distinguish between the inherent growth impulse in the jaws themselves and the possible stimulus of growing teeth. Dr. Lansberger operated on puppies. He extracted at a very early age, before, in his opinion, they could possibly have had any influence in stimulating growth, the germs of the temporary and permanent teeth on one side of the jaw only. He allowed the puppies to live for some twelve months, then destroyed them, and examined the jaws. He found "that the changes observed were typical and constant. The direction of growth in the jaw was always altered so that a twisted or one-sided effect, difficult to describe adequately in words, was obtained. There were also evidences of inadequate development in certain parts of the bony skull, and a marked hypertrophy of certain parts about the nostrils was prominently in evidence," and so on. One knows that the effects of use and disuse are very great, and without seeing the specimens and without having a very full account of the experiment one feels that it is at any rate just possible that Dr. Lansberger may have attributed to extirpation of the tooth-sacs facts which were really due to use or disuse. We have very recently seen some results of the extraction of teeth at an early age in man. Those of us who were present at the Royal Dental Hospital on Saturday afternoon saw some extremely interesting cases of this kind. It has appeared to me for some time that the effect of the early extraction of teeth on the growth of the jaws is very little. If one extracts temporary teeth early the other teeth will come together and the dental arch will be crowded; but I am not at all convinced that there is any lack of growth in the jawbone proper, and I shall be very anxious to hear what Mr. Colyer can tell us about that from his experience. Then there is another cause which has been given for lack of growth and for perversion of growth.

In December, 1910, Dr. Rollinson Whitaker read a paper at Birmingham before the Midland Counties Branch of the British Dental Association, in which he attributed a great deal of the dental irregularities which occur to-day to thyroid insufficiency. He is in the habit of looking at the regulation cases in the hospital at Birmingham, and he noticed these cases were correlated with nasal obstruction. Then he began to look at all his cases of nasal obstruction, adenoids, enlarged tonsils, and so on, and out of 800 cases of nasal obstruction he found that roughly 50 per cent. had perfect dental arches. Thirty per cent. were, in his opinion as a medical man, urgently in need of treatment and regulation, and the remaining 20 per cent. he classed as indifferent.



By that I imagine he means that there was irregularity, but it was in his opinion slight. That is an exceedingly interesting statement, because it tends to show that nasal obstruction has not anything like so large a share in the cause of dental irregularities as some of us have been inclined to think. He noticed, moreover, that the worst dental arches did not by any means always occur where there was the worst nasal obstruction, and he found bad arches where there was very little nasal obstruction, and a great deal of nasal obstruction with good arches. He pushed his researches further, and he asked the parents of his patients to what they attributed this throat trouble of their children. Many of them did not attribute it to anything—had not noticed—but a certain number of them had, and they almost unanimously attributed it to some illness—measles, or one of the exanthemata—from which the child had suffered. They further said the child had never been the same in health since. In this latter group were found practically all the cases which he had previously classified as having thoroughly bad arches. Seeing these two conditions so often related, he began to search for a common cause, and found it, in his opinion, in thyroid insufficiency. He came to the conclusion that nasal obstruction acting on arches which had not grown sufficiently hard owing to thyroid insufficiency was the cause of the irregularity, and that if a child's growth was perfectly healthy the jaw was able to withstand the action of the nasal obstruction, whereas if a child was suffering from thyroid insufficiency the nasal obstruction was too much for it. I wrote to Dr. Whitaker and asked him if he would kindly let me know what had been his experience within the last two years, and whether he had confirmed the opinion he expressed two years ago. He replied as follows: "All the evidence I have collected during the last two years tends to confirm the views I put forward in the paper you refer to, and I am more than ever satisfied that thyroid inadequacy is the essential predisposing factor in these cases. Since that paper was published I have had the opportunity of observing a considerable number of cases of dental irregularity, not drawn from hospital classes, and whenever a case was brought up for treatment earlier, the results were even better than in those from which my original observations were drawn. On the practical side, experience has taught me that even smaller doses than I originally used are indicated, and that the best results all round are obtained by giving them for a long period. Most of these children have been put on half-grain 'tabloids' of fresh thyroid extract, twice daily, for about six months." That is very interesting, and I think a good many of us must have felt for a long

time past that the fundamental causes of irregularities of the teeth and jaws lie very much deeper than the mechanical factors to which they have been attributed hitherto.

Another observer, Dr. Leonard Williams, finds contracted arches in all cases of thyroid insufficiency.

Orthodontic cases fall into two great divisions:—

- (1) Where the use of appliances is impossible.
- (2) Where the use of appliances is possible.

Division (1) must be treated by extraction or "immediate" regulation, if at all; therefore a thorough knowledge of this method is imperative.

Division (2) allows of choice, and with it this discussion is concerned.

Here I should like to take exception to the application of the term "mutilation" to extraction undertaken for orthodontic purposes. It is a term of opprobrium. It is a term which is used to create bias in the same way as anti-vivisectionists use the term "vivisection." Any surgical operation is "vivisection," but one does not usually so describe it in scientific circles: and I fancy that the gentlemen who describe extractions for orthodontic purposes as "mutilations" probably do not describe their own extractions so, but only other people's. Now, there are certain general principles which govern the extraction of teeth for orthodontic purposes, and it is desirable that everyone should thoroughly grasp them. It is quite impossible for the poorer classes to obtain orthodontic treatment, and therefore they should be treated in the only way possible—namely, by extraction. In private practice cases are conditioned by circumstances. We have to consider the child's temperament and health, we have to consider whether the child is accessible or whether it is inaccessible, whether it is at school or not. We have to consider further, the amount of time which can be given up to the case, and we unfortunately have to consider the fee which the patient is able to afford. So that each case has to be taken on its merits. Whereas treatment by mechanical means may be suitable in one case, treatment by extraction may be more suitable in another, and it very often happens that a combination of both methods of treatment is the best.

The condition of general crowding where the relations of the lower to the upper jaw are normal (Angle's Class I) is always due to lack of growth, and it may or may not be accompanied by adenoids and by an ill-developed nasal cavity, but a child may be perfectly well and strong,

even well grown for its age, and yet we may find this lack of growth. Where the lower jaw or the lower arch of teeth is backward in its relation to the upper arch (Angle's Class II), there may be perversion only, or there may be lack of growth as well. The interesting thing about it is that it is always foreshadowed in the temporary dentition. Moreover, if post-normal occlusion be present in the temporary dentition it will always be found in the permanent dentition. I believe it may be discovered very early in the life of the child, and I am very anxious to know how early, also the normal position of the jaws at the time of birth. Some time ago I wrote to a number of medical men who I thought ought to know something about what a child looks like at birth, and asked them if they could tell me what was the normal relation of the lower jaw of a newborn babe to the upper, but they none of them knew. I firmly believe that this is a condition due to some faulty growth, the cause of which operates very early in life, probably during foetal life. There is a tendency to ascribe these conditions to mouth-breathing and lack of use of the tongue, but they may occur without either. It is quite common to find children with post-normal occlusion who breathe perfectly well through their noses, who never have been mouth-breathers, who have been breast-fed, who have been well all their lives, and are well grown for their age, and I am sure that the condition is a hereditary one. I do not think one ever fails to find a history on one side or the other, either in the father's family or in the mother's family, and very often in both. And here the theory of thyroid insufficiency does not seem to me to come in, because there are no other symptoms. The condition occurs in children who are absolutely healthy in every other respect and who present no other abnormality.

Now as to treatment, first of Class I—the treatment of the crowded mouth where the jaws are of normal relationship. The treatment may be by means of extraction. Either you may extract some of the teeth and so get the others into reasonably good occlusion, or you may expand the jaws and so provide room for all the teeth in their normal positions. In deciding which method to adopt one is very apt to overlook the fact that the child has to grow, that the small arch which appears suitable to its face when it is young will not be suited to it when it is grown up, and there is no doubt in my mind that the effect from the æsthetic point of view is very much better in the majority of cases if expansion be adopted rather than extraction. I do not say that it is so in every case, but it is so in the great majority of cases. Now these cases are very frequently associated with lack of growth of the nasal cavity. Can we, as we are

told by some people, stimulate the growth of the jaws by expanding the alveolar processes? Can we stimulate growth which will increase the size of the nasal cavity? This is an exceedingly important question. Mr. Oppenheim has been doing some work which is of very great value on this subject. He took a young ape and regulated its teeth on one side, leaving them unregulated on the other. On the regulated side he pushed teeth out, he pulled them in, he twisted them round, he lengthened them, and he shortened them, and after six weeks or so he killed the ape and cut sections of its jaws. He found an exceedingly interesting condition. He did not find that absorption and deposition which we lazy theorists have believed in for so many years. He found very marked changes throughout. He found, on examining the alveolar process on the side which had not been interfered with, that the bony trabeculae were parallel with the long axis of the tooth. When he put sideway pressure on a tooth and pushed it at right angles to its long axis, he found that absorption and deposition were both going on at the same time in the bony plate against which the tooth was being pushed, and in that from which it was being pushed; that the whole architecture of the bone was altered, and that the trabeculae from being parallel with the long axis of the bone became horizontal to it. If the pushing of the tooth causes all that disturbance, and all that rearrangement in the architecture of the bone, surely we may very reasonably hope that the moving of the whole arch of teeth, or expansion outwards, would cause a very considerable rearrangement of the bone at the base of the alveolar processes. Of course we know quite well—there is no doubt about it—that the growth of the alveolar processes can be stimulated by expanding the teeth, and I think it is not unreasonable to believe that the bone of the supporting jaw may be to some extent influenced—that having arranged our teeth in a wider arch and somewhat altered the strains which are to be taken by the bone of the jaw, that that bone should rearrange itself to take the strain.

People have claimed—and for all I know quite truly—that if one expands the upper jaw rapidly one is able to separate the bones on either side of the median suture. If that be so, does it widen the nasal cavity or does it not? I suppose that it must. The objection has been put forward that the amount of widening can be but very small. That is true, but if it takes place at all, if you get, we will say,  $\frac{1}{8}$  in. of separation, it seems to me that that will have a considerable effect upon the ease of breathing. It is not very much—it is only  $\frac{1}{16}$  in. on either side—but it is spread over a considerable

vertical distance, if you imagine the outer wall of the nose swung outwards like *this* (indicating). That would make a considerable difference to the amount of air which enters. The whole cavity of one's nose is filled through a comparatively small orifice—the nostril—and the amount of space which would be gained, compared with the orifice of the nostril, seems to be quite considerable. We all know that when we have a cold and get exceedingly stuffy, if we snuff up menthol we obtain a certain shrinking of the mucous membrane and we get a little air in. We get through a small chink a very considerable amount of air. I should be glad to have the opinion of any person who has tried this method as to whether it is or is not possible to divide the upper jaw at the suture in this way, and if the result is worth while. It has been objected that we have no means at our disposal at present to measure the amount of widening of the nasal cavity, if any widening does take place. That is true, but it seems to me that it ought to be quite easy to discover this much at any rate, whether the child can breathe more easily than before or whether it cannot. If these claims are true, if growth can be stimulated by the moving of teeth, if the nasal fossæ can be widened, then, undoubtedly, one should adopt expansion treatment rather than extraction whenever possible. The argument about appearance does not seem to me a very strong one, for the reason that so very few people have trained eyes. I do not think a layman notices whether a person has lost a premolar or whether he has not, although it may be perfectly obvious to the trained eye. Moreover, there are many people nowadays who like to see small mouths. It may be a vicious taste, but it exists. After all, their appearance is only being improved for their own sakes and not for the sake of the people who do it; and if they are satisfied with the smaller jaws, and if it is equally good for them, then I do not see why we should take a great deal of trouble to expand them merely on considerations of æsthetics. Stimulation of growth is a different matter.

Now as to the treatment of the Class II cases—the cases where the lower jaw is in posterior relation to the normal. What are the pros and cons here? There is the question of the restoration of facial symmetry to begin with, and in these cases there is no doubt that the patients often prefer to keep what they call the family characteristic. They have been accustomed to have rather prominent teeth and rather narrow jaws. A great many people like to preserve that character rather than to change it for one they are not accustomed to in the family. Now as to the methods of treating this class of case. You may treat it in two

ways. You may either extract some teeth, probably the two first premolars from the upper jaw and draw the anterior teeth back and so accept the faulty position of the mandible, make the upper jaw a little faulty too and draw it back to fit the mandible, or you may advance the mandible and the teeth. I am supposing for the purpose of argument that we have one of those cases where the jaws are well developed as regards size, where there is plenty of room for the teeth, and there is only that alteration in the normal shape of the arches which is necessary to enable the lower arch to occlude with the upper when it is a little farther back from the normal. Supposing one treats that by means of reciprocal traction—by drawing the upper teeth back and drawing the lower teeth forward—what happens? Three things may happen. One may not affect the position of the upper teeth at all, but draw the mandible and the teeth upon it forward by the width of one bicuspid tooth. Then you would have the patient's chin protruding to that extent, and you would have the profile improved by that extent. But it is very doubtful whether one can do that without altering the upper teeth at all, and the result, I think, more usually than not is that the upper teeth come back a little and the lower teeth come forward a little, and the result is something between the two. That is the second thing that may happen. Probably in that case the chin may be moved forward the distance of half a bicuspid. Then there is the plan which some people adopt of tilting all the upper teeth back without advancing lower teeth or mandible. There we get to very much the same condition of things with regard to the upper jaw as would have arisen had the two premolars been extracted; that is to say, the lower jaw remains where it was—the third possibility. The gain even of a bicuspid tooth in the forward position of the lower jaw is not very great, and I very much doubt whether that is ever gained. Moreover, I am inclined to think that when one has succeeded by reciprocal traction in getting normal occlusion, there is no permanent alteration in the position of the lower jaw. I do not believe the lower jaw is altered in shape or that it stays in the forward position into which it has been drawn. Here are three bad photographs which illustrate my point. This child suffered from post-normal occlusion and her teeth were drawn into normal occlusion. This is before the child was treated; her chin is rather far back. As a matter of fact, her centrals were projecting over the lower lip. She was then treated, and her jaw brought into the position shown in the middle picture. There it looks as if her chin was more forward than before. The next photograph shows her a year afterwards. Her teeth are still in normal



occlusion, but the chin has reverted to the old position. Where the arches are at all contracted it is highly desirable to expand them, and I believe that the great majority of these cases are best treated by expanding the lower jaw to the full, by expanding the upper jaw to fit it, and then extracting the two first premolars and drawing back the anterior teeth. I think that treatment is much less lengthy than "jumping the bite," and I think it has the advantage of being more permanent, and less time and trouble are required to be spent on retention. I think one can feel more certain of getting a permanent result by this method than one can from the other, and that, supposing everything has been properly carried out, one loses nothing by it. The only thing is that the patient is one tooth short, he has one bicuspid less than otherwise; but in these days of cooked food I do not think the loss of the area of two premolar teeth in the whole mouth counts for much. Moreover, if one draws back the upper teeth, if one pulls back the molars in the upper jaw, it seems to me that the eruption of the wisdom teeth is bound to be hampered. I do not mean to say there are not cases where one has no doubt whatever that the proper thing to do is to restore normal occlusion. That is especially the case when the teeth in the upper jaw are none too far forward, and one cannot afford to draw them any farther back and where there is a deep overbite.

Now, what is the best age to expand the jaws? I am quite sure it should be done early. I do not agree with those who believe in exceedingly early regulation, regulation beginning at 3 to 4 years of age. I have been obliged to do it in one case, but I never want to do it again. It seems to me that one gains all one needs if one begins at about the age of 7 or 8 years. I do not think it should be delayed beyond that age. There is no doubt that early treatment has very great advantages. One is that it is very much easier. The jaws expand exceedingly readily while the temporary molars are in position, and these form exceedingly convenient attachments for one's apparatus. It is done with no trouble to the child, and I believe the result is permanent. I like the age of 8 years, because it allows me to use the temporary teeth for retention. I know that if the plates by any chance are not kept properly clean they will do no harm, because they are anchored to temporary teeth only which will be lost, and the arches are expanded just at the time when the premolars are ready to come down. One can guide those premolars into position and get an extremely good result with very little trouble at this age.

Now we come to Class III. This is where the lower jaw is pre-



normal to the upper. This is a very striking drawing by Leonardo da Vinci. It shows exceedingly well a thing which is very apt to be forgotten—namely, that associated with abnormalities of the dental arches are very considerable abnormalities in the jaws themselves.

One hardly ever sees a Class III case where there is not some great lengthening of the chin or forward obtrusion of the chin, and that alone, I think, is sufficient to indicate that the cause of irregularities of that kind lies very much deeper than anything which affects merely the arrangement of the teeth. So far as I know that cannot be explained by any theory of nasal obstruction. It is also hereditary so far as I can discover, and it is practically always associated with this particular growth of the jaw or with some such condition. Here our only chance, so far as I know, is to use a chin cap with strong elastic bands on it going to a cap over the back of the head when the child is quite small. Then I think one may have some chance of altering the growth of the mandible and so improving it, but it has not yet fallen to my lot to do so.

Lastly, I would ask, does the remedial effect of dental orthopædic treatment extend beyond the dental arches? To what extent may it contribute to the health of the individual? Can one expect to improve the health of a child as well as its appearance? Inasmuch as we can improve mastication it is so, and sometimes one has seen in small children who have come with the lower arch biting entirely inside the upper an enormous improvement in health when one has expanded the lower jaw. I should also like to have the opinion of the meeting as to what extent the breathing of the child can be affected by means of dental treatment. Great things are claimed for it on the other side of the water, but I should be very glad to have some proof.

#### DISCUSSION.

Mr. NORTHCROFT said he desired to draw attention to the very grave danger there was of oral sepsis in those cases where teeth had been extracted. Cases of Angle's Class II, Division 1 (superior protrusion), often accompanied, as they were, with mouth-breathing, were the first to show signs of periodontal disease, and he thought the orthodontic treatment should be looked at from this as well as from the æsthetic point of view.

Mr. STEADMAN said that he did not believe that the mere presence of teeth in the jaws could normally act as a stimulus to growth, because, if that were so, superior protrusion could be brought about at will by the simple process

of extracting the lower six-year-old molars in a young child and inferior protrusion by the early removal of the upper molars. In either case the jaw from which the teeth had been removed would show a deficient development, while the other jaw, retaining the full number of teeth, would grow normally. Experience proved that, in spite of the extractions, both jaws would develop to the normal extent.

Mr. WYNNE ROUW said he desired to put before the meeting, in the short space of time at his disposal, some points in orthodontic treatment as they appealed to him. Mr. Badcock had, for reasons which he (Mr. Wynne Rouw) could not understand, made no mention whatever of the fact that the extraction of the permanent teeth was a cause of mal-occlusion. In his own practice of several years' experience, both hospital and private, he had seen many cases of orthodontics, and he had reason to believe that the utter disregard for what might follow the removal of good permanent teeth was one of the most prominent factors in the production of mal-occlusion. In that connexion it was the six-year-old molar which was the poor tooth which was usually condemned to an untimely end. Fifteen years ago he had the advantage of reading a paper written by Dr. Isaac Davenport, having special reference to the point in question, and it then struck him very forcibly that perhaps he had, like many more, been erring, and so he promptly determined to test for himself the conclusions at which Dr. Davenport had arrived. He thereupon took impressions of every case in private practice which showed missing six-year-old mandibular molars, and the result in each case was the same—a complete disorganization of the bite. Mr. Badcock had drawn a distinction between hospital and private cases, but he took it that the members present were chiefly concerned with patients who were paying them fees, and for that reason it was well that they should weigh very carefully the question of the extraction of the permanent teeth. With regard to the cases which Mr. Badcock had placed in Class II, he desired to take very strong exception to certain of the conclusions which had been arrived at. Mr. Badcock, in speaking of those cases, had gone quite contrary to the teaching of the orthodontics school in America. He thought Mr. Badcock would admit that to Dr. Angle was owed the sound footing on which the science of orthodontia was placed. Dr. Angle, who had seen tens of thousands of cases, and had recorded his impressions, had undoubtedly arrived at the fact that in regard to the cause and effect, especially as applied to Class II, adenoids had to be regarded as one of the prominent factors in the production of the deformity. He could not agree with Mr. Badcock's statement that the best interests of the patients could be served by expanding the jaws and extracting certain teeth. In his practice and teaching he had always stated that it was the duty of orthodontists to, as far as possible, follow the plan which Nature had given them to follow, and their efforts should be directed, whenever possible, to *restoring* occlusion rather than to *improving* it, and for that reason "jumping the bite" was the correct and proper treatment. He understood Mr. Badcock did not believe in that method, and in support of his view he had thrown a picture on

the screen showing a single instance where a relapse had occurred after following out this line of treatment. "Jumping the bite" was an operation conducted every day, and there was no question of relapse, provided that reasonable care and control be exercised in its accomplishment.

Mr. HARRY BALDWIN said Mr. Badcock's remarks were excellent but very wide, and he thought a better purpose would have been served if the discussion had been directed to the consideration of modern orthodontic practice, and ætiology reserved for another discussion. As, however, so much had been made of causation, he desired to say that personally he thought nasal stenosis or difficulty of nasal breathing caused by adenoids and enlarged tonsils was, in the great majority of cases, associated with the irregularities which were the result of crowding, and in his opinion there was a very distinct relation between them. In such cases the first thing to do was to see that the adenoids and diseased tonsils were removed. In cases of post-normal occlusion he thought probably both conditions existed with regard to the jawbone—namely, that there was altered growth and diminished growth. The alteration in the direction of the growth, which was chiefly manifested by the lateral alveolar processes being pressed together, was due, he believed, to mechanical effects. The mouth being held open, the tension of the cheeks was increased on the outer side of the lateral alveolar processes, while the pressure of the tongue on the inside was diminished by the falling down of the tongue together with the lower jaw. That would necessarily cause an alteration in the direction of a growing and plastic bone, and would result in the lateral alveolar processes being pressed together. He believed the diminished growth was largely correlated with the impaired functioning of the nasal apparatus. With regard to modern orthodontic practice, he thought the great difference which existed between that and the orthodontic practice of years ago was in the retaining in a great many cases of all the teeth, the expansion of both jaws, and the frequent use of fixed apparatus, which apparatus mainly consisted of bands fixed round the molars supporting wire bows round the dental arches, and reciprocal traction. In his view, that method in the great majority of cases was an exceedingly valuable one and marked a great advance. The results obtained by it were far better from every point of view than those which used to be obtained by the old methods of extraction without expansion. He did not think it was sufficiently recognized by operators, when reciprocal traction was used, to what an extent the upper six-year-old molars actually travelled back, and not by way of being tilted. In estimating what could be done in regard to the retaining of the teeth and bringing protruding incisors back, one had to remember that a certain amount of space would be got in the upper jaw by the six-year-old molars actually going back. The cases which had given him the most satisfaction, especially from the æsthetic point of view, had been those which had been treated by the preservation of all the teeth and the complete regulation of bites and size of arches by means of expansion and reciprocal traction.

Mr. J. G. TURNER said Mr. Badcock asked for opinions about the possibility of insufficient mastication. As the members had heard in Mr. Badcock's remarks, he (Mr. Turner) had seen some hundreds of cases of idiot children, who had been fed on nothing but pap, and whose jaws were not only well formed but larger on the average than those of an equal number of normal children. There were also tribes in Africa, the children of which were suckled from two to two and a half years, and immediately they began to feed simply bolted their food without using their teeth at all. The process of feeding was to cook yams in a certain way, roll the food into balls varying in size from 1 in. to 2 in. in diameter, dip the ball into some liquid fat or oil, put it into the mouth, and it could be watched going down the gullet. There was no use of the teeth, yet the jaws were large and well formed. The same remarks held to a lesser extent with regard to the Arabs. Such facts put aside all argument as to expansion by mastication or failure of growth owing to want of mastication. Mr. Badcock raised the question of the premature extraction of temporary teeth. It related to any teeth extracted prematurely. A contracted arch was obtained of necessity because the pressure of the lips and cheeks worked on an arch, the members of which had no resistant power of themselves and no support but soft bone and the futile tongue. Until the bones were hard enough to resist the pressure of the lips and cheeks there was always distortion of the arch by reason of early extraction. With regard to thyroid insufficiency, it was of course probable that in certain cases the failure of growth of bone in stunted children was due to thyroid insufficiency, but to say that failure of growth in a child who was well grown in every other respect except the upper jaw was due to thyroid insufficiency was, to his mind, nonsense. Yet that was the condition in which most children came to them. They were not poor, stunted, little children, they were by no means wanting in vitality. Their sole failure in many of the cases was in the upper jaws, and that was a point which might be correlated with the failure of growth of the upper jaw which occurred in congenital syphilis. In both cases a picture was presented of a very subacute inflammatory stasis of all the nasal mucous membranes, and consequent on that it was quite probable that there was lymphatic stasis, and failure of nutrition of the parts, so that the bones failed to grow. As to the observations of Dr. Whitaker, his figure of 50 per cent. of perfect arches would probably resolve itself into a much less percentage when looked at by an expert, especially considering that a number of those cases showed but very slight deformity when looked at by anybody except perhaps the parents and the dentist. With regard to bad arches with very little or no obstruction of the nasal breathing, that was distinctly in opposition to his experience, and he might say to the experience of the rhinologists he knew in London. The argument as to measles which Dr. Whitaker had produced might be put in exactly the opposite way—that the measles were due to the general failure of resistance caused by the sepsis, and to the failure of filtration by nasal breathing. With regard to the cases which came in Class II, his experience was that there always was an actual failure of growth in post-normal occlusion,

except in certain instances which were most obviously congenital, if not hereditary. He thought it was possible to separate those out by noting the growth of the maxilla as compared with the mandible—normal growth of the maxilla and a subnormal mandible—and in some cases by finding a true hereditary history. As he had said before, it was a common condition in animals and appeared to be very easily reproduced, though in what proportion of the offspring he could not say. He had found that the inter-canine width in acquired cases always showed that the lower jaw could not get forward into its proper position because the upper was too narrow to receive it.

Mr. NORMAN BENNETT said he differed from Mr. Turner's argument against function stimulating growth. Idiot children who had been brought up on pap food might have most excellent jaws, but he wanted to know a great deal more about idiots than either Mr. Turner or anybody else knew about them before he could accept such cases as reasonable examples to draw conclusions from with regard to ordinary people. Mr. Badcock, in his opening remarks, had asked whether post-normal occlusion was not due to very deep-seated causes. He thought it was obviously so, and that before the real cause was discovered orthodontists had to define the means of distinguishing between one kind and another. Post-normal occlusion was no more one disease than rheumatism and measles were the same disease. He was quite sure that in many cases there were different conditions. He had in mind, for instance, on the one hand the kind of case in which there was a very narrow upper arch, in which the patient certainly had adenoids, and in which the lower jaw could not by any possible means be brought forward without expanding the upper arch. On the other hand, he had in his mind the sort of condition that his own eldest child, aged 6, had. In that case there were no adenoids, there had been nasal breathing from infancy, and there was a rather abnormally wide upper arch, but, as Mr. Turner had said, there was obviously some defective growth from the condyles, and the upper incisor teeth tilted backwards. In speaking of the treatment of cases of post-normal occlusion Mr. Badcock rather leant towards rejecting the treatment by expansion and intermaxillary force—he (Mr. Bennett) used that phrase in preference to "reciprocal traction." It seemed to him that one had to distinguish the different cases in deciding upon the treatment, because obviously in that comparatively large class of cases in which with the post-normal occlusion the upper incisors were all tilted backwards (that was to say, where the lower lip had got outside and not inside), if a premolar was extracted a worse tilting backwards of the upper incisors would result than had been the case before treatment, because there would be great difficulty in moving back the roots of the teeth to the extent of more than one unit.

Mr. DOLAMORE thought that whatever might be the cause of the size of the jaws when one child in a family might suffer from some mysterious disease whilst the others did not, the fact remained that, taking a large family, one child would often be found with a totally different type of jaw from that of the other children, and yet its teeth would not be dissimilar from those of its

brothers and sisters. Among his patients was a family of three; the eldest, aged 19, was a little dot of a girl with a very small and narrow, but, having lost six premolars, a regular dental arch. The teeth of these three sisters were of the same type. They were all healthy children, and why was this one child so short? The father was short and the mother was tall. The two younger children distinctly took after the mother and the eldest took after the father. It would be found that in many families one child would take after one parent and the rest after the other parent, and in his experience the teeth did not vary in the same way. He had two models with him which showed a difference in width between the two first upper molars of at least  $\frac{1}{2}$  in., yet the front six teeth were of precisely the same size. In another model there was a difference of  $\frac{3}{4}$  in. between the molars. There was only a difference of slightly over  $\frac{1}{4}$  in. in the measurement of the six front teeth.

Mr. BADCOCK, in reply, said that Mr. Rouw had spoken of the extraction of teeth, especially the first permanent molar, as being a cause of mal-occlusion. He thought that treatment was as dead as Queen Anne. Mr. Rouw gave a great deal of credit to Angle, and some was due to him, but he thought Angle was wrong in a great many of his theories, and he did not in the least agree with the theory that adenoids or nasal obstruction always accompanied cases of post-normal occlusion. It did not. He could produce half a dozen cases in which there was well-marked post-normal occlusion with protruding teeth, and there was no nasal obstruction of any description. He agreed with Mr. Bennett that there were many separate varieties of post-normal occlusion. With regard to Mr. Rouw's remarks about the case he had shown on the screen, it was not a case of relapse. The bite was jumped and remained jumped. The point was that the chin returned to its old position. What doubtless happened in all these cases was that the upper teeth moved slightly backward, the lower teeth moved slightly forward, and the relation of the jaws remained as before, or eventually came to be as before. He agreed with Mr. Baldwin as to the necessity of operating for adenoids. Mr. Turner's remarks on African tribes were exceedingly interesting, and contributed a great deal to the knowledge of the subject. Mr. Turner seemed to have confused the contracted arch with the contracted jaw. He (Mr. Badcock) was quite aware that if one extracted teeth the dental arches became contracted. The point he wished to elucidate was whether it had any effect upon the body of the bone. He agreed with Mr. Turner that a large number of the cases could not be due to thyroid insufficiency. In many cases, such as that of Mr. Bennett's child, where the only fault seemed to be in the upper jaw, it was ridiculous to think of thyroid insufficiency. He did not know whether Mr. Turner meant to suggest that in those cases a history of syphilis was generally found. [Mr. TURNER said No; he was only drawing a parallel.] Mr. Badcock, continuing, said Mr. Dolamore's remarks were exceedingly interesting. Many cases no doubt were cases of heredity. Post-normal occlusion was such a common thing that it might be called a variety of normal.



## Odontological Section.

January 27, 1913.

Mr. P. SIDNEY SPOKES, President of the Section, in the Chair.

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### Discussion on Orthodontics in Modern Practice.<sup>1</sup>

MR. COLYER, in opening the discussion, said that they, like Mr. Badcock, were anxious to have a more thorough knowledge of the causation of irregularities, for upon that, to a very large extent, depended their rational treatment.

With regard to the question of growth of the jaws there were certain well-ascertained facts; for example, there was very little doubt that there was an intimate relationship between nasal obstruction and want of growth of the maxillæ, but what the exact relationship was, was not very well understood. One view held was that the want of growth in the maxillæ could all be explained by the want of function arising from nasal obstruction. On the other hand, there were those who maintained that the nasal obstruction was often secondary to the want of growth of the maxillæ, the want of growth of the maxillæ being associated in some way with thyroid inadequacy. A very important point, on which our knowledge was still deficient, was the influence of the teeth on the growth of the jaw. It was important to arrive at more correct views on this subject, as on it was based the operation of expansion of the arch. In trying to arrive at a conclusion as to whether the teeth did influence growth of jaw, there were certain facts to be considered. First, there was reason to think that the tooth and the surrounding capsule was a separate entity from the body of bone itself—this view was in some degree supported by a specimen of a malformed sheep, with fusion of the orbits, in the Odontological Section of the Royal College of Surgeons Museum; in that specimen the terminal tooth, with its bony capsule, projected into the zygomatic fossa. Secondly, there was a specimen of a young manatee, which also seemed to suggest that the tooth and its bony capsule was quite independent from the rest of the bone. Then, again, in specimens showing absence of teeth there was, as a rule, no want of growth of the body of the bone in the region from which the teeth were absent. Quite lately, too, Dr. Keith had described a skull of an individual, aged 18, who had suffered from progeria. In this specimen the maxilla was very little more developed than that of a newborn child, but the permanent teeth had gone on to full growth,

<sup>1</sup> Adjourned from November 25, 1912.



and were arranged in an extremely regular manner. Lastly, with regard to the experiments of Lansberger, he thought that the deformities described in the skulls could possibly be more accurately explained on the lines of use and disuse. The general conclusion he (Mr. Colyer) had come to was that there was very little evidence to show that the teeth in any way influenced the growth of the jaw.

In considering, too, the question of the jaws of the present race one must not lose sight of the fact that there has been a greater decrease in the length of the jaw compared to the size of the teeth. This is well illustrated by examining the jaws of modern Europeans, and comparing them with those of uncivilized races, and also by a consideration of the different breeds of long- and short-muzzled dogs.

With regard to the question of the relation of early extraction to the growth of the jaw, he pointed out that one must clearly keep in view the effect on the arch, as separate from the effect upon growth of jaw. There was undoubtedly, of course, a definite effect upon the arch from early extraction. The effect of early extraction upon the arch depended on the time the teeth were extracted and on the degree of crowding of the growing teeth. His experience was as follows: In extraction before the age of 6 there was a movement forward of the permanent first molars, especially the upper, the moving forward being more marked in jaws where there had been retarded growth than in normally developed jaws; that in early extraction after the first permanent molars are in place there was very little forward movement if the jaw was normally developed; on the other hand, if there was want of growth, or retarded growth, of the jaw a movement forward of the molars took place. Lastly, there was one other point to be remembered in dealing with the question of growth: In the past many of the observations had been made upon abnormal mouths, that is to say, patients showing want of growth of the maxillæ: at the present time a large number of children presenting normal mouths were being brought to practitioners, and thus an opportunity was being afforded of studying the jaw growth under normal conditions. And the impression he had formed was that the jaw grew very much more than they had been led previously to believe.

With regard to treatment, the question resolved itself into one of "expansion" or "extraction." Now the problem that they had to deal with in crowded mouths was a want of growth of the jaw—in other words, the jaw was insufficiently developed to accommodate the normal number of teeth. Those who advocated expansion believed that spreading the arch did stimulate the growth of the jaw; but, as he had pointed out, there was very little reason for believing that this took place. The main point in favour of expansion, to his mind, was the æsthetic one, and also perhaps the sentimental one of trying to retain the allotted number of teeth. Against expansion he felt there were strong disadvantages, one of which was the direct damage to the tissues from the apparatus, and secondly from the septic processes set up around the teeth. Extraction, on the other hand, if carried out with due regard to the occlusion,

and at the proper age, gave excellent results without any mechanical interference; and even if the process of extraction did result in slight æsthetic defects, he thought that disadvantage was outweighed by the gain of avoiding sources of sepsis.

Mr. Colyer referred, too, at some length, to those cases in which the upper teeth occluded in front of their normal position, and stated that he thought this condition was due really to a movement forward of the upper arch, rather than to a want of growth of the mandible; and, believing this, he thought that the most rational treatment was the removal of a premolar and the retraction of the anterior teeth. He showed models in which the operation of intermaxillary reciprocal retraction had been carried out, and had resulted in the second upper molars, which had been previously functional, being forced back so as to become practically functionless.

Mr. G. NORTHCROFT said that he believed in extracting teeth where necessary. It was a little difficult to understand the title of Mr. Badcock's paper, and he thought it had led to some confusion of thought; but he would confine his remarks to what he believed would be germane to the general subject. He only wished to deal with such types of cases as, in his opinion, could not be possibly treated by extraction, and he wished to show that there were *some* cases in which extraction was not a panacea by any means. The speaker held that Mr. Badcock wrongly assumed, what was so generally held, that extraction was a method of treatment for all cases. After hearing Mr. Colyer's remarks that evening, one would think that he was prepared to treat any case that came along with forceps; and Mr. Northcroft maintained that it was an absolute impossibility to treat some cases rationally with forceps. If Mr. Badcock's remark, "that it was quite impossible for the poorer classes to obtain orthodontic treatment, and that they could only be treated in one way, by extraction," meant anything, it meant that extraction was not orthodontic treatment, and there he failed to agree. He wanted to endorse a statement of Mr. Badcock's, that the extraction of teeth would rarely be sufficient treatment in itself. One must supplement that treatment by further mechanical means, and when one had become proficient in the use of fixed appliances, he thought it was just as easy to use them as to extract teeth. He himself had drawn attention to the importance of a study of the irregularities of the temporary dentition some years ago; and he found on further study that practically all types of irregularities that occurred in the permanent dentition were foreshadowed in the temporary dentition, except such as were obviously created by too early loss of the teeth. It was most important that the function of the teeth and jaws should be considered. If they could put their patients' teeth in efficient occlusion, he thought they would be doing a very good thing for them; and he was of opinion that the more efficient the masticating apparatus the less chance there would be of periodontal disease. He could not quite see why Mr. Badcock left the expansion of some cases so late. Of course, they knew that Mr. Colyer said that if a young case was treated successfully it might as well have been left alone, because it was really Nature that had done

the work. He, however, was thankful to feel sure that sometimes he had assisted Nature after all.

The question of early treatment must necessarily depend on the type of patient. He did not think it was possible to teach that one could treat all these cases very early; but he thought, in a large number of cases of lingual occlusion of the upper temporary teeth, for instance, by expanding the arch at an early age they did get the normal width of the permanent arch established, and established early with definite growth of bone in the palate. He quoted a case of inferior protrusion that had been treated at the age of 2 years 11 months, and the case was still quite satisfactory. It had also to be remembered that early expansion of the temporary arch had the advantage of expanding the underlying permanent teeth that were held between the roots. Mr. Badcock believed in expanding the arch at the age of from 7 to 8; the speaker thought the absorption of the roots of the temporary teeth having begun, such a good effect could not be obtained on the surrounding structures. He exhibited some slides which showed, in a boy aged 9½, first the disastrous result of the extraction of all the temporary teeth in a case in which the lower jaw was already post-normal; also, six months later, demonstrating how much worse the case had become. The mandibular molars were in post-normal occlusion; the first left mandibular premolar also; the left permanent canine was biting in between the lateral and the first premolar, and there was no room for the maxillary canine to erupt. Also he gave a side view of the case as treated, and then three years later; and he had brought down the models of the case when the boy was aged 15, so that one could see that there was a permanent result with the normal number of teeth in the mouth. He also produced further models, one being a case of marked post-normal occlusion, certainly the worst case he had ever seen. The boy at the age of 10 was thought too delicate to undergo orthodontic treatment—he was not surprised at this view, because he must have had only two cusps of his lower molars for use in mastication, but he pointed out the result of the case treated by the expansion of the lower jaw. One was satisfied in simply bringing the lower jaw into normal occlusion and giving the patient an efficient masticating apparatus. The last case he showed with rather mixed feelings, because Mr. Colyer's methods had been to a certain extent carried out (not by himself), and they would perceive the result. In a case of post-normal occlusion with fan-shaped lower incisors, Mr. Colyer advised, he believed, the extraction of one of the incisors, and subsequently or at the same time the upper first premolars. This treatment was going to be carried out in that case; at any rate, the lower incisor had been extracted, and they could see for themselves that the mandible was too small, and the extraction of a lower incisor simply made it smaller, and all four premolars in the upper jaw might as well be extracted if the upper jaw was to be reduced to the present size of the mandible. He thought, in the subsequent treatment of this case, the first premolars would now have to be lost. The case certainly brought out the danger of being too dogmatic about one's methods, and the necessity of taking broad views when discussing "Modern Orthodontic Practice."

Dr. SIM WALLACE referred Mr. Badcock, in connexion with the latter's question as to whether mastication had any effect on the growth of the jaw, to a paper by Dr. Laurence Baker. Dr. Baker made experiments on young growing rabbits by filing the teeth on one side of the mouth in such a way that mastication was impossible on that side, leaving the rabbits to masticate on the other side. He was able not only to show that the jaw on the side that was not functional did not grow as well as the side that was functional, but also that all the bones on that side of the face, and right up to the base of the skull, were similarly affected through the lack of mastication on that side. But perhaps more important than the direct results which were evidenced from these experiments was the indirect effect of lack of mastication. In the case of a child or any other person only able to eat on one side, it would be noticed that, on the side that was eaten upon, the teeth were more or less clean, while the teeth on the other side were dirty. So we concluded that when food not stimulating mastication and the self-cleansing processes of the mouth is eaten, the mouth becomes what is called septic. Various secondary results then followed, the child became delicate and emaciated and the tongue shared in the emaciation. Bodily development did not progress satisfactorily and the jaw did not grow so well when the food was not of such a nature as would compel mastication and stimulate the self-cleansing of the mouth. The question of heredity did not lend itself to discussion in a few minutes; but the speaker wished to indicate what Mr. Badcock's views seemed to involve, namely, the assumption that abnormalities were inherited with greater certainty than normalities; for if such abnormalities were only inherited in equal proportion to the normalities, then the proportion of pre-normal and post-normal cases would not be any greater to-day than it was fifty or a hundred years ago. It was, however, extremely difficult even to maintain the abnormal characteristics of a prize pigeon, for example, through any number of generations. The tendency was always to reversion to the normal. He thought with regard to the question under discussion at the moment, it would lead them into the most painful absurdities to maintain that all cases of pre-normal or post-normal occlusion were inherited. There were many possible factors which might bring about such a thing as post-normal occlusion. He would only mention one that he had formerly referred to at the British Society of Orthodontics—namely, the peculiar instinct to gnaw which an infant had before and during the time of the cutting of its incisor teeth. At that age there was an incessant tendency for the child to gnaw everything that it could get its hands on. He now believed that the rationale of this was that at a very early age indeed there was a provision of Nature for the correct occlusion of the incisor teeth. The lower jaw was habitually held in the position that was most suitable for gnawing, and the bones at that age readily adapted themselves to that position. In other words, gnawing was an instinct which produced at a very early age the first correct occlusion; and it was quite possible that children brought up very properly according to present-day teaching, that is to say, with no comforter, no bottle-feeding and no

mouth-breathing, might yet have been deprived of every possibility of putting anything in their mouths which would lead to correct occlusion. He maintained that before they claimed that heredity was the cause of all cases of pre- or post-normal occlusion they should investigate certain environmental factors which it was in their power to modify or control.

Mr. F. ST. J. STEADMAN: I have studied and endeavoured in my early days of orthodontic practice to carry out several different methods of treatment, but as a result of my experience now limit myself to one system—namely, that taught by Mr. J. F. Colyer, because to my mind it is the only system, based upon an intelligent appreciation of the aetiology of the irregularities of the teeth, and therefore, as one would expect, the one giving by far the best results in practice. Let me take for example a case of superior protrusion due to adenoids and mouth-breathing, or in other words to nasal obstruction. According to Professor Keith the growth of the maxilla depends upon the increase in size of the antrum. Mr. Mayo Collier in a post-graduate lecture delivered a year ago points out that there is a regular tide of air entering and leaving each of the six chambers which open into the nasal cavity—viz., the frontal sinuses in front, then farther back the anterior and posterior ethmoidal sinuses, below the antrum of Highmore, posteriorly the sphenoidal sinus, and, lastly, the Eustachian tube. He notes that all the openings are directed away from the inflowing stream of air and face directly the outflowing stream. He tells us that the reason for this is that each of these cavities is filled during each expiration and the amount of air is then lessened during each inspiration. He proves this statement by quoting a case in which he removed a button of bone in the mid-frontal region in a healthy human subject, leaving the lining membrane of the frontal sinuses intact. He found that this lining membrane sank down markedly with each inspiration and was blown out with each expiration. My own opinion is, and I gather it is also the opinion of Mr. Mayo Collier, that the growth of the antrum depends largely upon the constant slight pressure of this outflowing stream of air, occurring as it does twenty thousand times a day. Mr. Mayo Collier goes on to point out that if the air during inspiration cannot pass through the nasal chambers it must pass through the mouth, and in doing so abstracts part of the contents of the nasal chambers, lessening the tension of the air in the chambers, and exposing all the walls of the nasal box or palate and approximates the outer walls, so squeezing the alveolar arches together, thus forming the high and narrow V-shaped arch with which we are so familiar in these cases, approximating the turbinal bones to the septum and throwing forward the front portion of the alveolar arch and with it the incisor teeth. As a result of these factors the maxilla is not properly developed and this lack of development is chiefly shown where the growth is most active, that is, in the molar region: consequently there is not sufficient room in many cases for the first permanent molar to occupy its normal position and it lies, as Mr. J. F. Colyer points out, with a general slope backwards. When the second

deciduous molar is lost, therefore, the first permanent molar moves forward by swinging in the arc of a circle, the centre of which is situated about the end of the anterior root, and so comes to encroach upon the space left for the premolars. When the permanent canines erupt, if they can force their way into the arch in the insufficient space which is left for them, the result must be a further throwing forward of the incisor teeth. The final result is simply this, we have a deficient development of the maxilla, but we have the normal number of teeth, and moreover these teeth are normal in size.

What, then, is the logical treatment of such a case? To my mind it is this: First of all, we must endeavour, as far as possible, to bring about an increase in growth and expansion of the upper arch, not by inserting expansion plates, but by calling to our aid the forces which normally bring about the growth and expansion of the bone. This can be done by the removal of the nasal obstruction and rendering the nasal cavity again functional, but unfortunately patients come to us too late for this treatment to correct the deformity entirely. Considering that the real trouble is that there are too many teeth for the ill-developed jaw, it is to my mind only logical to sacrifice two of the premolars, one on each side. Having come to this conclusion, it seems to me illogical to wait until the permanent canines have erupted and done the mischief before commencing treatment; it is surely far better to carry out the treatment so strongly supported by Mr. J. E. Colyer—viz., the removal of the unerupted first premolars. The canines then, as pointed out by him in a post-graduate lecture, delivered at the Royal Dental Hospital some three years ago, seem, as it were, to drop bodily backwards and to erupt in the place which would otherwise be occupied by the first premolars. The pressure of the lips easily and surely correct the protrusion of the incisors. It has been urged by some as an objection to this line of treatment that the growth of the maxilla will be still further retarded owing to the loss of the stimulus to growth due to the presence of these teeth. I am quite convinced in my own mind, however, that the mere presence of teeth in the jaws does not normally act as a stimulus to growth, because if this were so we should be able to produce a superior protrusion at will by the simple process of extracting the lower first permanent molars in a young child, or an inferior protrusion by removing the upper molars, and this we cannot do. The final result of a case so treated is that without the insertion of any mechanical appliance we have the upper teeth in excellent occlusion with their antagonists; the superior protrusion is corrected, and moreover there is no tendency whatever to recurrence. One has to count up the teeth to find out that anything has been done. This, to my mind, is as near a perfect result as it is possible for us to obtain.

I perform this operation in my own practice at the age of 7 to 8, if I am so fortunate as to see the patient early enough to be able to choose the age. If the lower incisors are fan-shaped and impinge on the upper I do not hesitate in bad cases to remove one of these, and in slight cases to grind them down. In cases which come to me too late for this treatment, I remove



the first or second premolars—whichever is indicated, according to the severity of the lesion. I then follow Mr. J. F. Colyer's teaching in waiting a year to see how far natural forces, such as the pressure of the lips and tongue, will bring back the protruding teeth before inserting an appliance. It is surprising what these forces will do. Here again there is no tendency to recurrence, since these forces actually tend to correct the deformity rather than to increase it.

May I mention a case treated on different lines? Five years ago a handsome woman, aged 30, consulted me. She had a very marked superior protrusion. She had been treated at the age of 12 by one of our most distinguished dental surgeons, who had inserted a plate to pull back the protruding teeth. She wore this for two or three years, after which it was abandoned. The condition promptly recurred, and at the age of 25 she consulted another dentist with a very urgent request for him to do something, as she is, and always has been, extremely sensitive over her deformity. He having induced the teeth to go back slightly, inserted a fixed retention appliance by boring a hole in the labial aspects of both central incisors. He then inserted two pins into these cavities, which were attached to a gold wire carried back to a band round the first right molar. When I saw her five years later I found that the wire impinged against the interdental papillæ, between all the teeth on the right side from the first molar to the left central incisor. Food débris, resulting in a filthy condition, had naturally lodged behind this wire, which I, of course, removed: pus was streaming from deep pockets around each of these teeth. I saw her again a week ago; pyorrhœa alveolaris has now spread round the whole of the upper teeth on both sides. What has this patient gained from these two dentists? From the first, nothing—since the teeth occupy to-day the same position as they would have done had no treatment been carried out. He failed, because he had attempted to coerce the natural forces which placed the teeth normally in the arch, instead of finding out the cause of the failure of these forces and removing it. As a result of what was done by the second dentist, she contracted a disease which has caused her marked general ill-health which will continue until all the upper teeth are removed.

In conclusion, the principle which I endeavour to carry out in my own practice is, first, to find out, if possible, the cause of the irregularity with which I have to deal and to try to remove it. Secondly, I call to my aid the natural forces which place the teeth in the normal arch instead of opposing them as so many kinds of treatment advocated do; such opposition must lead to disaster. Thirdly, I prefer to sacrifice a tooth on each side if by so doing I can avoid an appliance. Fourthly, I *never* use fixed appliances because they cannot be kept clean. Fifthly, I avoid, where it is possible, unfixed appliances because it is extremely difficult to make the young patient realize the great importance of cleanliness and because most appliances lower the efficiency of mastication at an age when most rapid growth is taking place and therefore when it is most needed. I have seen them used in delicate children suffering from phthisis, where a judicious extraction would have done all that was necessary and left the child fit as far as its mouth was concerned to combat the much



more serious disease. Lastly, for these reasons I prefer immediate regulations where such a course is feasible. I feel that I cannot too strongly condemn the unnecessary use of mechanical appliances.

Mr. E. STURRIDGE thought there could be little doubt that expansion of the arch stimulated growth of the alveolus, and with it growth of the jaw, in children. Proceeding, he remarked that two slides exhibited by Mr. Northcroft seemed to him to illustrate that point: in the first (before treatment) a contracted undeveloped mandible was seen, while in the second the same case after treatment appeared much larger, with evidence of a good deal of development of the alveolus, and he took it that the jaw had also developed. The stimulation of growth of the alveolus was not confined to expansion; it also occurred in retraction cases, and took place in adult life as well as in children. He did not agree with Mr. Colyer's principle of extracting teeth which could be brought into proper occlusion and retained there, to be functioned by a bony process which readily developed on being stimulated in the manner referred to. He passed round photographs of models of a case of a patient, aged 27, in which the superior incisors protruded to the extent of about 2 cm., and were loose in a thin, diseased alveolar process. After retraction to the normal position, the alveolar process had developed on the labial aspect to a remarkable extent, the pyorrhœa had completely disappeared, and the teeth were now held in a well-developed alveolar process after fourteen years. The development of the alveolus due to stimulation occurred in adult life up to the age of 45, as far as he had tested it, and probably took place much later.

Mr. RUSHTON, while appreciating Mr. Badcock's paper very highly, felt he must disagree with his definitions. There were only two causes producing irregularity of the teeth—viz., lack of development, and perversion of development, or a combination of these two. Mouth-breathing probably caused lack of development and perversion; thumb-sucking probably caused perversion only. As bearing on Mr. Colyer's remarks with regard to the lack of mastication, and also as regards the effect of the growth of the teeth on the jaws, he afterwards exhibited photographs of a boy and girl, and models of their jaws. The boy had never had any teeth, either temporary or permanent. The only teeth which had erupted in the girl were three second permanent molars, and, curiously enough, the upper and lower molars on the left side were in correct occlusion. In each case the bones of the maxilla and mandible were of average size, in fact, the mandible of the boy was particularly well developed, showing that at least the development of the bones of the jaws was not dependent on eruption of teeth or pressure of mastication. Both children had healthy appetites, were not restricted in their diet, and seemed to suffer no inconvenience as regards digesting their food. The models of the boy he had presented to their museum, and the case of the girl was taken from a paper of Dr. Courrier in the *Dental Cosmos*.<sup>1</sup>

<sup>1</sup> *Dental Cosmos*, Philad., 1911, liii., pp. 768-777.

Mr. H. CHAPMAN supposed he should be included also with the new school, but he would like to say that he did not consider himself bigoted in any way, and he was open to perform extractions if they really were for the benefit of the patient. Regarding the age of treatment, he felt that probably Angle's teaching would be much more to the point had he advocated treatment some eight to ten years earlier than he did in all his writings. The speaker's experience was that at the age of 6 one could use either removable or fixed appliances with comparative ease, just as easily as at 12 years of age. The movement of the teeth was certainly easier; and what was more important, the retention was simplified very considerably. He gave an example, and other cases he had treated had shown similar results. In those cases in which the lower jaw was too far back and the incisors were protruding, the overbite was so very considerable, in many cases the upper and lower incisors were in contact, that he would like to know how Mr. Colyer proposed to move those upper incisors, after removing two premolars, without any other treatment whatever. He dealt at some length with Mr. Colyer's argument that the lower jaw was in its normal position in certain cases, and that it was the upper jaw which had moved forward and was at fault; also that the upper teeth were sloping; and said that he could not accept the argument, because it seemed to him that the teeth were in their proper position, as regards vertical direction, in the jaw. He believed it was the lower teeth that were too far back, and that by bringing them forward, by mesial movement of the lower jaw, their vertical direction would be unchanged.

Mr. GEORGE THOMSON thought they must admit that the modern note was prevention, and in order to understand this they must get back to causes. Mr. Badcock's paper began by telling them something about causes, lack of growth, &c. Then he told them that one of those causes was constitutional disease, such as rickets. There the speaker wanted the modern teaching to come in, which was that rickets was not a constitutional disease. If they meant by "constitutional" that it was inborn, no child was ever yet born with rickets. The lecturer had referred quite briefly to Dr. Sim Wallace's statements and work with regard to insufficient mastication and disuse as causes for irregularities of teeth, and that was waived aside by an assertion of Mr. J. G. Turner that idiots, who were a very small proportion of the population, and were fed on pap, had well-developed jaws and teeth. That was no argument whatever against the other side, firstly because there were so few of them, in proportion to the population, and secondly he would like to ask whether it was not true with regard to idiots that one of the curious things about motherhood was that if a child was of that character it got more care and attention than other children, and the child was usually breast-fed; and that alone was sufficient to account for their well-developed jaws and teeth, as they saw among the Jews and savage races. Why should they want all these ingenious, complicated investigations to discover something that was quite simply understood? He concluded by disassociating himself from the argument of heredity to account for irregularities of the teeth.

## Odontological Section.

February 24, 1913.

Mr. P. SIDNEY SPOKES, President of the Section, in the Chair.

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### Hypertrophy of the Gums in a Child, aged 6.

By A. E. IRONSIDE, M.R.C.S., L.D.S.

I HAVE ventured to show this case because the condition is one of some rarity. As you will see on examination, since the patient is



Hypertrophy of the gums in a child, aged 6.

present, the temporary teeth are almost entirely covered by gum, there being but very small portions of the crowns projecting. When the jaws are closed the alveolar processes of the maxilla and mandible are in contact for practically all their length—a small depression exists in the front of the mouth and is due to finger-sucking. The opposed surfaces appear capable of performing efficient mastication. There is no family history of similar cases in ancestors or collaterals. There are five other children in the family, one of whom is younger than this child; all of them are normal. No history of syphilis; one miscarriage occurred before the birth of this child. The mother makes mention of a fright which she received during the middle period of gestation. I have models of the case and also stereoscopic skiagrams taken by Mr. Clark.

#### DISCUSSION.

Mr. IRONSIDE, in reply to the President, said that the parents did not know when the condition first started; they said that the child had never had any teeth.

Mr. STANLEY BOYD said that Mr. Colyer had sent him three cases in three brothers. They were not quite so extreme as the case of Mr. Ironside, but otherwise the trouble was the same. He treated the cases by cutting through the gum just above the edge of the alveolus on both aspects, baring the teeth and edge of the alveolus, and getting off the periosteum there. In one patient the condition recurred and he performed a second operation. When he last saw the case the result was satisfactory.

The PRESIDENT (Mr. P. Sidney Spokes) inquired if Mr. Stanley Boyd remembered Mr. Christopher Heath's case, which he treated by free removal. The patient was an adult.

Mr. STANLEY BOYD said that Mr. Heath had two cases, one of which he saw. In it the gums were quite soft and the teeth were all loose. Evidently the condition was due to some fairly acute infection. He thought Mr. Heath's treatment of the case was perhaps the only one which could be adopted. Mr. Heath used a pair of Liston's sugar-nipper forceps, and there was not much left when he had finished.

**Fibroma of Maxilla.**

By L. STANLEY KETTLEWELL, L.D.S.

THE patient was first seen in May, 1912, for a large swelling in the mouth; he was a dairyman by trade, and his age was 32. He gave the following history: Two years previously an attempt was made to remove what I judged to be the right maxillary second molar. The tooth was broken and the roots left behind. A swelling soon formed, which he was told was an abscess. He was advised to poultice it, and this he did for two years. As it steadily increased in size under this treatment and as the teeth in front of it were loosening, he returned for further treatment, and the swelling was incised. No pus was obtained, so he decided to go elsewhere for treatment, and thus came under my care.

When I saw him the right side of his face was greatly swollen and the skin of the face was slightly red. On examining his mouth I found it in a very septic condition, there being a considerable deposit of tartar on the teeth, with advanced periodontal trouble. There was a large swelling involving the alveolar ridge on the right side of the maxilla, extending from the tuberosity to the second premolar. The swelling was firm and tense, feeling almost cartilaginous, and the gum covering it was of a purplish-red colour. There was no visible sign of swelling in the antrum, nor did the patient feel any pain save a slight discomfort due to the size of the swelling. There was no glandular enlargement.

After thoroughly scaling and cleaning the teeth the patient was sent to the local hospital, and on June 10 the right maxilla was removed. The specimen shows a dense, firm growth in the alveolar region, with a freer-growing and less dense mass in the antrum, which has been practically obliterated.

*Patho-histological Report by Mr. Hopewell-Smith.*—Sections of the growth exhibit a dense, firm structure, consisting of well-developed connective tissue, certain cellular elements, blood-vessels and lymph spaces (fig. 1). The homogeneous connective tissue fibres are morphologically identical with those of normal fibrillar connective tissue, which is characterized by the close connexion and regular arrangement of its bundles. Running, for the main part, in thick, coarse, slightly wavy strands, and elsewhere in loosely distributed interlacings, they form the



FIG. 1.

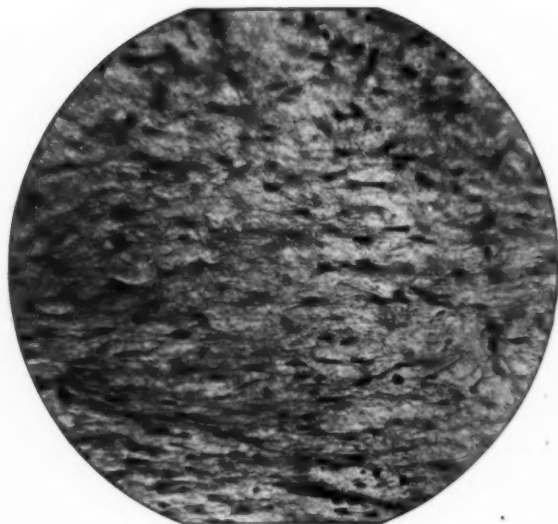
Fibroma of maxilla. General structure. ( $\times 250$ .)

FIG. 2.

General structure of the youngest portions of the growth. ( $\times 250$ .)

predominating feature of the tumour. The cells are relatively few in number, except in the younger parts. They include fixed connective-tissue elements, often folded upon themselves. Their nuclei are laterally compressed, and appear as narrow bands of compact chromatin. Leucocytes may be detected. In the newly formed portions the cells partake of an embryonic nature, and their nuclei are large, prominent, rounded or oval (fig. 2). The chromatin of the latter presents a well-marked reticulum, and one or more nucleoli may be occasionally seen. On the growing border of the tissue mast cells can be found, as may also be a few large lymphoid cells. The scanty blood-vessels generally show the ordinary microscopical structure; but, at times, a thickening of the middle and external coats necessarily leads to a narrowing of their lumina. Minute nodules of bone exist in places, and probably represent small detached outgrowths from the osseous antral wall, as well as degenerative changes occurring in the substance of the tissue. The epithelial lining of the antral mucosa of the sections examined is histologically normal.

Mr. STANLEY BOYD said cases of fibroma of maxilla were exceedingly rare; he could remember only one, a case which had passed through Mr. Underwood's hands. It began as an alveolar growth which Mr. Underwood removed two or three times. Then it invaded the antrum, and when he (Mr. Boyd) saw the patient, a young woman, aged about 25, the antrum was most obviously enlarged. It was quite an easy operation to shell the non-infiltrating growth out of the antrum and, so far as he knew, there was no recurrence. He supposed that the involvement of bone in Mr. Kettlewell's case necessitated a much more extensive operation.



### A Case of Odontome.

By H. J. RELPH, M.R.C.S., L.D.S.

MR. HERBERT RELPH said it had occurred to him that a case of odontome was of sufficient rarity in one's ordinary practice to warrant his bringing it before the members. This was a case of a composite odontome which represented the right lower third molar. It presented the usual symptoms which occur in such cases. The patient was a young man, aged about 27, who had suffered from several attacks of swelling and suppuration about the right angle of the lower jaw. The two right lower molars had been removed on different occasions, as they were thought to be responsible for the suppuration, and abscesses had been opened both from inside and outside the mouth. When the patient came under observation there was a good deal of brawny swelling about the angle of the jaw, and limitation of movement. There was a scar under the angle of the jaw, where an abscess had been lanced at one time, and a suppurating sinus in the sulcus. There was also a point at the summit of the alveolus which was discharging, and a bony point could be felt protruding through the gum. An exploring instrument revealed the fact that this bony point was only a part of a considerable mass embedded in the jaw, and as the tissue was of such density that a sharp probe would not penetrate it, it was thought probable that an odontome had to be dealt with. The patient was put under an anæsthetic, the jaw was opened, the gum incised, the bone chiselled away, and the mass which the members saw before them was shelled out without any very great difficulty. All suppuration had since ceased, and the recovery was quite normal. He had not had sections cut at present, as the specimen might be considered of sufficient interest to be placed in the Museum, and he thought the members might like to see it before the Curator cut any section he thought fit.

Mr. DOUGLAS GABELL hoped the specimen would go to the Museum, as it was an excellent one of a very definite class of odontome—what used to be called the ordinary composite odontome. The structure of such odontomes was quite marked. If sections were cut it would be seen that they did not vary very much in their method of being built up. He was sure Mr. Colyer could make great use of such a specimen if he was permitted to make sections.

## **Restoration after Surgical Operations.**

By GEORGE H. BERWICK, L.D.S.

DURING the last few years in my connexion with the Appliance Department of the Royal Dental Hospital, I have had the opportunity of seeing a considerable number of patients requiring various forms of apparatus, for the restoration of congenital defects, or for mechanical treatment after surgical operation. At the suggestion of some of my friends I have been induced to bring under your notice the experience which I have gained in treating these cases. I do not claim that what I have to place before you is original, but I thought that by recording the difficulties I have encountered it might be of help to those engaged in similar work. For my own part, I hope that in any discussion that may follow I may be able to perhaps obtain some fresh ideas which may assist in dealing with similar cases.

It may be convenient to group the consideration of the cases under headings :—

### **CONGENITAL CLEFT PALATE.**

There are two different classes of patients with cleft palates met with in practice :—

- (I) Those for whom no surgical operation has been performed.
- (II) Those for whom some type of plastic operation has been carried out.

#### *Class I.*

In connexion with Class I, I think it is almost agreed that the obturator is the best method of treatment. The velum, which used to be in vogue some years ago, answered its purpose well, but it has many disadvantages, e.g. :—

- (1) The extreme difficulty of obtaining a correct impression, as both the lower and upper parts of the cleft have to be modelled.
- (2) The impressions when obtained are not easy to make models from.
- (3) The very limited life of the velum, which may be estimated roughly at about eighteen months.
- (4) The septic condition into which it is liable to lapse

Turning to the obturator—and this term is used to denote an appliance consisting solely of hard substances—the method I adopt is as follows :—

(1) *The Impression.*—I take the impression of the hard part first, and never attempt to model the cleft at the same time. There seems to me no advantage in attempting to model the hard and soft palates at the same time; in fact, there is a great disadvantage, inasmuch as the sides of the cleft in the soft palate may be pushed into any position. Also with the introduction of a foreign material the soft palate may contract in an unnatural way. The varied movements of the sides of the cleft on its being touched have to be seen to be appreciated.

(2) *The Denture.*—In constructing the denture, several points must be borne in mind: (a) *It must be steady*, and the first point to consider is the amount of movement to be overcome, due to the tendency to displacement in the act of swallowing when the obturator is in place.

In some young mouths, stability may be obtained by the judicious use of cribs, but where the shape of the teeth or the bite does not allow of this, I think it is quite justifiable to remove one or more teeth. It is essential, if possible, to fit clasps well forward in order to resist the upward pressure of the tongue on the obturator, and also adjust some clasps towards the back of the denture to resist the downward and forward movement of the soft palate. With regard to the type of clasps, wires seem to be the most suitable, and this is especially the case with cone-shaped teeth.

In edentulous mouths one has to depend on springs, although in one case recently seen a patient retained a large obturator in place without their aid, but it may be noted that he had worn an obturator for some years previously, and during that period the apparatus had been secured by clasps around three teeth. These he had lost at different times, and had accustomed himself to retain the denture without their aid. One curious point in this case was that the obturator was rather high, and through absorption of the alveolar ridge it had gone up until it came to rest on the inferior turbinate bones.

Having noted the clasps necessary, the only difference from constructing an ordinary denture is to vulcanize a piece of gold wire in the denture extending from the heel of the plate long enough to reach to the extremity of the cleft. The advantage of constructing the denture first is that it can be fitted and the bite adjusted, so that there is only the obturator to trouble about. I might mention here that if the cleft extends into the hard palate it is only bridged over, and not carried into the depression.

Assuming that the denture is correct, we proceed to model the cleft. Take a mass of softened composition, dry, and wrap round the wire extension, making sure that the wire is hot so that the composition will stick firmly; let this mass be more than will be necessary to fill the cleft, pass into the mouth, and either syringe or give the patient something to drink. The sides will be marked by the walls of the cleft, the lingual side by the tongue, and the end by the superior constrictor. The mass should then be removed and trimmed until the composition is in the plane of the soft palate. When replaced in the mouth there will be a space between the margins of the cleft and the soft palate. Now the object of the obturator is to close the space completely between the oral and nasal cavities during the elevation of the soft palate, and to attain this end it is necessary for the margins of the soft palate to be always in contact with the obturator. It is therefore necessary, in the first place, to add material until the margins of the soft palate lie in contact with the obturator. This being obtained, care must be taken to see that the soft palate is also in contact with the obturator during the elevation of the soft tissues; any gap that may exist being filled up. As a method of practice, I find the simplest way to get the patient to swallow is to place the head fairly well back and then to squirt a jet of cold water on to the back of the tongue. Attention should be paid to the junction of the hard and soft palates, as any undue pressure at this point seems inclined to make the cleft gape. It should be mentioned here that the view of completely filling the cleft is not in accord with the view of most practitioners. It is generally taught that the obturator should only be of sufficient size for the sides of the palate to come in contact during the act of swallowing, the contention being that the sides are liable to ulceration. Mr. Colyer has for years filled the cleft entirely, and in several of these cases which I have seen after the lapse of years I have not noticed any sign of trouble in the soft parts, nor have I been able to elicit from the patient any history of discomfort. The obvious advantage of entirely filling the cleft is that there is far greater improvement in the speech, as it acts almost like a velum.

Having obtained the composition model, it now remains to make the hollow box. The case is invested in a large flask. The denture can be almost entirely covered, and the plaster brought flush with the top of the composition. The upper part of the flask is then filled in. In packing, after warming and picking out the composition, the hollow in the lower half of the flask, and also the part in the upper half that will form the lid (after thoroughly drying) should be covered with

freshly made chloro-rubber. The wire which held the composition can be cut back fairly close to the heel of the plate, but should not be entirely dispensed with, as it forms a useful method of strengthening the union between the two portions of the apparatus. The part where the obturator joins the plate should be roughened and have holes drilled for holdfast. The rubber should be packed (one thickness) inside the whole box, including the lid, except at the junction and end of the box, where it should be slightly thickened, as it is not unusual to have to ease the obturator at these points. There are two methods of keeping the box hollow. One is to place in the box just before closing the flask a few drops of alcohol, the other is to fill the entire box with dry pumice; this needs care, as some of the pumice may get into the junction of the lid with the box. If pumice is used it is necessary after vulcanizing to drill a good-sized hole into the box and shake the pumice out, and then to fill the hole securely with a vulcanite plug.

There is another style of obturator that should be mentioned, that is, one made like a trough. A good idea of this may be obtained by considering the box obturator referred to without the lid; these are not very satisfactory as they get filled with mucus and food.

When fitting in the obturator the patient should be advised to practise speaking slowly and distinctly, and if possible to read aloud for a certain time each day. In some cases, where patients have been a long time without an obturator, it almost means learning to speak over again.

The general result of obturators is extremely good, and patients soon get accustomed to the apparatus and their speech rapidly improves, and the voice appears to be stronger almost at once.

With regard to the age at which to introduce an obturator, there can, I think, be no doubt that the sooner it can be adopted the better, as the patients then early learn to accustom themselves to the apparatus. The disadvantage is the growth of the parts, the cleft becoming wider, needing occasionally a fresh obturator.

### *Class II.*

Those for whom some form of plastic operation has been performed. These cases are most difficult to treat to get a good result. One seldom sees a case where the operation may be considered entirely successful; of course, there is the possibility that those that are successful do not

come under notice, but, judging from those cases seen, the defects too often seen after operation are:—

- (1) The soft palate is not flexible.
- (2) A space exists at the back of the soft palate due to shortening.
- (3) The contraction of the soft palate seems altered, that is to say, instead of going upwards and inwards, it often seems to push downwards and forwards. In one case recently treated at the hospital, although the obturator was in the plane of the soft palate when at rest, on swallowing the sides climbed right over the obturator.
- (4) The uvula is generally hanging down in the cleft that remains, and when an apparatus is fixed the uvula is liable to become ulcerated.



FIG. 1.

Extension obturator.

In these cases it would be far better if the uvula could be removed before starting mechanical treatment.

From a mechanical point of view, most satisfactory results can be obtained by constructing an extension or fish-tailed obturator (fig. 1) as follows: Make the denture as for a box obturator, vulcanizing in a piece of half-round gold wire, with the oval side towards the palate, having the wire long enough to extend well into the cleft it is desired to fill. It is important that this wire, which has to bridge the space between the end of the plate and the cleft, shall not fit closely to the soft palate; in fact, this wire must be accurately adjusted when the plate is tried in. For this style of obturator I always have made a plate containing a wire strengthener that stretches across the heel of the plate, and the extension wire soldered to it, as it is essential that the plate and wire should be rigid. When the denture has been fitted

and found to be satisfactory, the space or cleft remaining is modelled with composition firmly secured to the wire extension, and the space filled as much as the patient can tolerate. It is advisable sometimes to start with a small obturator first to get the patient accustomed to it. The shape of this style of obturator depends on the conditions found, as they are very complex; it is not necessary to make it hollow, as more than often an almost flat plate of vulcanite is sufficient. In one case I made simply one thickness of rubber extending backwards to cover a small round hole that remained in the palate. In another case a wire bent to escape the uvula was tried, but curiously enough the patient preferred a previous plate where the wire went straight back.

#### RESTORATIONS AFTER REMOVALS.

*Apparatus applied immediately.*—This has been done on several occasions, by making a splint of metal to occupy as nearly as possible the space left after the operation, carrying it on to the sound part, placing in position and fixing with osteo before the skin-flaps are sewn up.

*Apparatus after Healing.*—The first essential in dealing with these cases is to obtain an accurate model.

*Moulding the Obturator.*—The following points should be borne in mind: Pressure on the soft tissues must be as far as possible avoided, and no attempt made to restore contours. A good plan is, suppose a portion of the maxilla is being restored, to get the patient whilst the modelling compound is in position to draw the mouth over to the normal side.

Retention of these cases is not always an easy problem. If possible clasps only should be used, but above all the apparatus must be steady. Springs, therefore, are usually necessary, as the weight of the apparatus (although made hollow) causes it to drop on one side. It is a good plan to cover the spring on the injured side with a piece of fine rubber tubing. It is not advisable, in my opinion, to attempt to obtain full masticatory value on the injured side.

*Restorations of the mandible* do not present quite the same difficulties as those of the maxilla, the principal difficulty being in overcoming the contraction of the tissues and the action of the unopposed muscles.

Passing from these general considerations, I will now deal with a few special cases:—

*Case I.*—The patient was a clergyman, aged 60, for whom both maxillæ had been removed with the exception of the floor of the right orbit. When



first seen the six lower incisors were standing, but as these were affected with periodontal disease they were removed. The patient was unable to make himself understood and brought his wife to interpret the sounds she had become familiar with.

The main difficulties of the case were :—

- (1) The unstable character of the tissue on which the denture would rest.
- (2) The marked contraction of the upper lip, producing a constant tendency to push an appliance backwards.
- (3) The extreme contracted condition of the soft tissues on the left side. The above condition of the tissue rendered it almost



FIG. 2.



FIG. 3.

impossible to obtain an efficient masticatory apparatus, and all that could be hoped for was a restoration sufficient to improve the appearance and speech. Impressions were obtained and the cases set up, but during the interval the wound had so contracted that the trial plate would not enter the orifice. Fresh impressions were obtained and an obturator made of black rubber, carried slightly into the hollow left by the operation and attached to the lower denture by springs (fig. 2). No teeth were attached to the upper denture, as it seemed desirable to get the patient accustomed to an apparatus, but on inserting this the pressure of the upper lip completely upset the stability of the apparatus. It was therefore determined to take the obturator

well into the cavity in the palate, extending it well over the tissues. By this means it was hoped to resist the backward pressure of the lip. An obturator made in this way proved most satisfactory and no harm accrued to the soft tissues (fig. 3). The patient quickly became accustomed to the apparatus and the speech rapidly improved. After wearing this for some time the patient thought his appearance might be improved by some teeth on the upper denture, and as the lower had become very unsteady owing to absorption after the extractions, a fresh set was made for him on the lines of the first one but carrying six front teeth on the upper (fig. 4). This seemed to improve

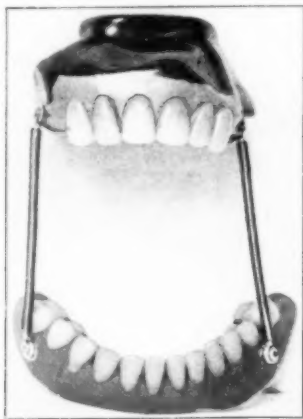


FIG. 4.

the speech even more, and when last seen the patient could read loudly and quite distinctly, and returned full of hope to his clerical charge at St. Vincent.

*Case II.*—The patient, a female, aged about 30, was to have the left half of the maxilla removed. Models of the mouth were obtained and a metal splint was made to fit over the teeth and portion of the palate which would remain, a skull was then selected with jaws of about the same size and a thick metal shield (copper) was struck up to a model of the facial surface of the maxilla. This shield and the cap were then soldered together, a stiff wire being soldered to the end of the shield and stretching across to the end of the palate piece. (See fig. 5.) This splint was fixed in position with osteo at the time of the operation before the skin-flaps were sewn up. After wearing this a few days it was found desirable to close the opening in the splint, and a

removable metal cover was made for this. The advantage of this splint was that it kept the parts at rest, and when the patient was seen a short time after the wound was scarcely visible; when deemed expedient this splint was removed and impressions taken. A hollow box obturator was constructed for the upper carrying teeth, springs being necessary; a small denture was made for the lower. The first permanent molars being absent, the swivels were easily attached. On the right side in the upper the teeth were intact and the swivel for that side was carried on a crib taken over and between the teeth.

This apparatus was worn for some time with perfect comfort, but contraction of the soft parts made a new set necessary, and when I last saw this patient she was perfectly happy with the restoration.

There is one point of interest in connexion with restorations of the maxillæ that may be noticed here—namely, that in this style of restora-



FIG. 5.

tion it is not unusual to get trouble with Stenson's duct. I remember a patient complaining that when she ate the saliva used to run down the nostril. On examination it was found that the duct lay just over the edge of the obturator and the box being dome-shaped the saliva found its way over this and so down the nose. This was corrected by cutting a hollow in the side of the case, in which the duct could rest, and also a channel down to the teeth, thus making a miniature aqueduct, or rather saliva-duct.

*Case III.*—This patient, a female, aged 19, came to the hospital for fillings. On examining the mouth it was found that there was a tremendous discrepancy between the upper and lower front teeth; and it was suggested that the mouth might be rendered functional by the removal of certain teeth and the insertion of a denture. This was readily agreed to, and  $\overline{5421} | 124$  were extracted and the gums allowed to heal;  $\underline{3} | \underline{3}$  were then carefully trimmed so as not to

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encroach on the pulp chamber or the gum margin, and cast gold caps were made and cemented on. The idea of retaining the canines and capping them was to give a bearing to the denture in front, and so help to resist the great



FIG. 6.



FIG. 7.



FIG. 8.

leverage that would otherwise be exerted on the molars owing to the discrepancy between the lower front teeth and the upper alveolar border. A vulcanite denture was then constructed with clasps on 63 | 36 and soldered

to a half-round wire strengthener, thus making a rigid plate, and the teeth brought out to meet the lower incisors. This proved very satisfactory, as it gave the patient additional biting power and considerably improved her appearance. The appearance of this patient hardly coincides with what one would expect on seeing the models. It was found that the patient had developed a habit which edentulous people frequently adopt—that is, when at rest keeping the tongue curled with the tip in the sulcus of the upper lip, thus keeping it out (figs. 6, 7, 8, 9, and 10).

I have put this case under restorations as it may be classed as a deformity, and where there is no occlusion, extraction of the teeth and a denture are the only hope of obtaining a satisfactory result.



FIG. 9.



FIG. 10.

*Case IV.*—The patient, a man aged 40, had a kick in the mouth from a horse; he placed himself under the care of an Indian nurse in Canada, with the result that the wound became malignant, and necessitated the removal of the lower lip and part of the mandible. When I saw him he was suffering from loss of masticatory power, as he had only one molar left on either side in the lower jaw. He also suffered great inconvenience from the saliva dribbling over the chin. There was some loss of teeth in the upper; these were made good by a denture. On examining the mouth I found that the patient possessed an extremely wide lower jaw; and as the mouth was very much contracted and the scar-tissue would not yield in the slightest degree, the problem was, how to obtain impressions. I proceeded as follows: Two lower trays were cut in half and each side of the mandible taken separately, the distance between the two

molars was measured with dividers, and the two half models set in a block as nearly as I could judge in the right position. To this model a tray was made with an adjustable handle. This tray was tried, and I found by closing the sides and then hollowing out the handles it enabled me to place it in position; composition impressions were then taken, and before removing the tray a scratch was made where the handles crossed, and the tray was then lifted up and the two halves approximated and withdrawn from the mouth. The handles of the tray being secured in the right position, a model was cast. To this model I had clasps made to the molars, and connected by a stout oval wire, soldering a loop to where I calculated the lip piece would come; catches were soldered to the wire where the teeth were to be placed and to this attachment composition blocks were fixed. It should be mentioned here that I was enabled to obtain an impression of the upper jaw by using a Britannia metal tray with the outer rim cut away. On trying the wire in the mouth, which necessitated passing it in sideways and then turning round, it was found to be hardly correct; the wire was then cut through at the point of the loop attachment and placed in position; soft plaster was then packed around this, and by this means I was able to obtain an accurate impression of the lip portion. The model was then sawn in half, the clasps and blocks sealed in position and the impression of the front part poured and incorporated with the two halves. To this model a denture was constructed, the missing part in front being restored by soft pink rubber. This was subsequently changed for ordinary pink vulcanite, which acted very well, and when last seen the patient was getting along well with the apparatus, and the masticatory power much improved.

#### *Adaptive Shortening of Lip.*

In hare-lip, especially after a severe operation, there is nearly always a shortening of the upper lip, with a tendency with time to get shorter. It has been found that if the lip is kept on a slight stretch that it prevents this, and so allows of a more æsthetic result when deemed advisable to make a denture. Mr. Colyer has several cases of this kind. One is a patient aged 7, who has hare-lip and also a gap in the right lateral and canine region. A simple vulcanite plate was made for this patient, with wires around the temporary teeth and the gap in front filled with a block of white vulcanite, which was carried as high as possible into the sulcus of the lip and left rather full. I saw a case quite recently where a patient had worn a similar denture, and it was remarkable how flexible the lip had become.

#### *Noses.*

The construction and adaptation of these depend on the amount of destruction of the tissues. Where there is only the loss of the nose to make good, it is usual to attach it to glasses.

*Taking the Impression.*—The patient is laid in the horizontal position, or nearly so, and the opening plugged with wool—the portion to be modelled and the wool plug are smeared with vaseline; soft plaster



FIG. 11.



FIG. 12.



FIG. 13.

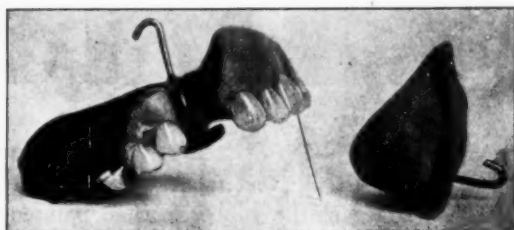


FIG. 14.

is then plastered freely over the parts and allowed to set. This is removed and a model cast, which gives the margins of the orifice, the lip, and the bridge of the nose. It is of great assistance if the patient



possesses a photograph taken before the nose was destroyed, as this gives one an idea of the size and shape to model the artificial one. A wax nose is then constructed, and in this is incorporated a piece of metal struck up to fit the nose in the position where the bridge-piece of the glasses will come. It is then tried on with the glasses and any alteration made that is deemed necessary. It is a good plan in ordering the glasses to mention that a wide bridge be constructed; two holes are then drilled through the metal and either scratched on the metal extension, or pins may be soldered into the metal, and so that when the restoration is finished it only remains to rivet this to the glasses. Being



FIG. 15.



FIG. 16.

satisfied with the wax model, this is then duplicated in white rubber. The surface of the rubber is then painted with oil paints and allowed to dry, the glasses being then riveted on, and the joint made good by the use of a little grease-paint. The restoration has been helped in one or two cases by the addition of a moustache; where this has been deemed advisable an extension of the vulcanite has been carried down over the lip, and the patient sent with the nose to Clarkson's, who have manufactured a moustache and sewn it on to this extension.

*Noses where a Perforation of the Palate is also present.*—In these cases a denture has been constructed carrying a wire hook which went through the perforation, and to this hook has been attached a rubber

ring; a piece of wire with a hook at the end has been vulcanized into the nosepiece, long enough to extend into the nasal cavity and nearly to reach the hook on the denture; a special button-hook has been made so that the patient could pass it into the cavity and catch hold of the rubber ring. By putting this on the stretch he has been able to attach it to the hook on the nose, and thereby keep the nose steadily in position (figs. 11, 12, 13, 14, 15, and 16).

In one case we tried making a porcelain nose on a platinum base and attaching it to glasses; the disadvantage of this was its weight. One difficulty experienced in this was that when the patient bent down the nose swung off its base, but this was overcome by carrying an extension into the nasal cavity.

In conclusion, I have to acknowledge my thanks to Messrs. Colyer, Dolamore, Gabell, and McKay for so kindly allowing me to refer to cases which have been under their care.

#### DISCUSSION.

The PRESIDENT (Mr. P. Sidney Spokes) imagined that most people who had any experience of such cases would prefer to fit an obturator in the maxilla rather than have to restore a missing portion of the mandible. Mr. Berwick had not dealt with the mandible except in the case where he had had to treat a deficiency in front of the mandible with a molar left on either side. But he imagined the most difficult cases were those where a large portion either right or left of the mandible had been removed, and it was desired to restore the missing piece. He thought good results generally followed the use of obturators for the maxilla; he had had more of those cases to deal with than mandible cases. He had brought to the meeting two old slides illustrating a specimen in University College Hospital Museum, in which a portion of the mandible had been removed in the front of the mouth. The great difficulty experienced in the mandible was the tilting in of the remaining sound side, which was drawn inwards by the muscles. The first slide showed, from the outside, what had happened in the lower jaw. The two halves had been what he might call approximated by Nature. Bony repair would be noticed in the front, where the middle line should have been. The result was perfectly functionless as regards mastication. The next slide showed the condition of things from the inside. Members would notice the middle line falling inwards. That was a condition of things which might be expected to occur if the patient lived long enough for ossification to take place, and if Nature was allowed to take her own course.

Mr. STANLEY MUMMERY said he had brought to the meeting a model of a case which had been sent to him a year ago by Sir Rickman J. Godlee just after he had operated on it. The man had an epithelioma starting in the sockets of the second upper right molar, and there was an extensive growth, necessitating the removal of the whole of the upper half of the right part of the maxilla,

including nearly half the palate and all the alveolus and teeth on that side as far as the laterals. Three weeks after the removal, when there was just a little mucous membrane formed—there was no actual bleeding spot—he made the patient a vulcanite plate covering the whole palate, with no teeth at all on the affected side. It would be seen in the model that there was an extensive hole where the palate had been removed, that went right up into the nasal cavity. The difficulty was with regard to retention. The patient had a lower plate, and springs were put in, but they caused such irritation on that side that he was afraid of doing damage and had to take them out again. He finally fixed the plate by clasps between the molar, the canine and the lateral. The restoration here was a solid block which was  $\frac{3}{4}$  in. to 1 in. thick. He had a solid piece of pumice carved out to form the block of the plate with a thin coat of vulcanite over it. He found it very successful. The plate was not heavy, kept up perfectly, and prevented regurgitation through the nose. Later on, when the tissues had altered, he made another plate with teeth on both sides, and the patient could now eat, drink, talk, smoke, and do everything he wanted to. The case was rather like the one which had been described by Mr. Berwick.

MR. H. LLOYD WILLIAMS said Mr. Berwick had referred to the method of taking the impression but did not pay any attention to getting an impression of the cleft. He (Mr. Williams) always preferred to get the most complete impression of the cleft possible—not that one was able to make any great use of it afterwards, but one knew where one was in building up the obturator. Instead of making the obturator as Mr. Berwick did, of modelling composition, he usually made it of wax with a small hard core, because he always endeavoured to fill up the cleft as fully as the patient could bear it, and the only way to find out what the patient could bear in that respect was to heat the surface of the wax, put in the apparatus, get the patient to swallow, and go on in that way, shaving a little wax off or adding a little wax as necessity arose, until the patient was able to swallow easily and the sides of the cleft and the superior constrictor and the pharynx slid easily over the wax. When that was done the apparatus was put forthwith into the flask for baking. He was convinced a patient was much more comfortable with a full obturator than with an obturator which did not reach far back. The difficulty of speech was very much less with a full obturator than with a smaller one. Mr. Berwick had not referred to the doming of the obturator. In his (Mr. Williams's) opinion the obturator should be so made that the tongue might find its correct contact as in pronouncing the letters "k" and "g." He quite agreed with Mr. Berwick in regard to velum. Kingsley made some very beautiful vela. They had, however, gone out of use at the present time owing to the fact that they were extremely difficult to make, and even after manufacture one found that, in some patients, at the end of three months they were so intolerably bad smelling that their use could not be continued. In his opinion it was always advisable to make the obturators early, say about the age of 6 or 7. He would like to know what experience members had had of attempts to improve the speech of patients. Kingsley said that the learning of a foreign language was a great aid, but he (Mr. Williams) had never been able to try it. What odontologists

had very frequently to deal with were restorations due to destruction from syphilis or other surgical operations. He agreed with the President in saying that mandibular cases were extremely difficult to deal with. After the mandible had been removed the patient perhaps suffered from bad mastication, but if one interfered there was often a recurrence of the new growth. He was quite persuaded that it was very much wiser to leave the mandibles alone in the majority of cases. The cases of restoration of the maxilla were very interesting, and although on the face of it one would expect a good deal of difficulty in many cases in holding up the apparatus after fitting, the apparatus seemed to disobey all physical laws and to stay up in the most remarkable manner. He had had a curious experience some years ago. A very well known clergyman came to him to have his maxilla and a portion of his cheek restored after removal for sarcoma. He made him an apparatus to restore his palate and the appearance of the cheek. After he had put the apparatus into the mouth he asked the patient if he could speak, and the first thing he did was to intone "Dearly beloved brethren." With regard to restoration of the nose, he had seen the case shown on the screen at the Royal Dental Hospital; it was a perfect success.

Mr. PEYTON BALY said Mr. Berwick had mentioned that there were two methods of filling the box. He desired to suggest a third method—namely, that instead of pumice stone ordinary whitening should be used, and after drilling a small hole, the box left in hydrochloric acid overnight. The easiest way to fill the hole was to tap a thread and screw in a piece of vulcanite.

Mr. A. T. PITTS said he desired to refer to a method advocated by Professor Pickerill in dealing with cleft palate. He performed a small plastic operation so as to make a narrow bar of tissue which bridged across the cleft about the middle of the soft palate. He then made a hook on the posterior surface of the obturator which went over the bar of tissue so as to give the apparatus greater stability. The method certainly sounded very ingenious, and Professor Pickerill said he had practised it on several occasions with great success. He (Mr. Pitts) could not help feeling, however, that the scar-tissue would probably not bear any very great strain. With regard to the case of the shortening of the upper lip in hare-lip which Mr. Berwick had described, he had had one such case to deal with in a small boy, aged 4, who had a complete cleft and double hare-lip. The boy was operated on at a very early age and several other operations followed. The cleft was closed, but there was a tremendous shortening of the upper lip; it came across in quite a straight line, and the teeth came through in a most hopeless condition. The two deciduous canines were separated by a space certainly less than  $\frac{1}{4}$  in. After expanding the canines he was able to put in a plate which stretched the lip very considerably and improved the facial appearance a good deal. It also had the effect of improving the voice to a slight extent.

Mr. W. W. GABELL said he would like to ask Mr. Berwick to what extent one might hope to get the restoration in speech, in cases where obturators were used. In those cases which had come under his attention the patient had been

able to speak well enough to be fairly understood, but the defect was still most pronounced. He did not know whether a higher standard than that ought to be attained; and he would like Mr. Berwick to say what standard of restoration of speech ought to be aspired to.

Mr. J. F. COLYER said he had read Professor Pickerill's article which had been referred to by Mr. Pitts, and it appeared to him that Professor Pickerill was doing to the cleft palate the very thing that he (Mr. Colyer) always desired to avoid. He, personally, always felt that he would like to cut away the piece of scar-tissue between the two halves of the soft palate, because in his opinion that was the very thing which interfered with the proper adaptation of the soft palate to the obturator. With regard to the improvement of speech, as a general rule the results varied very considerably, but there was a case Mr. Berwick had shown that evening in which he had never seen a better result obtained from the use of an obturator. He desired to refer to the method he had adopted for a number of years in treating children who had undergone operations for hare-lip. One of the great troubles which had to be overcome in making anything like an artistic appliance in after years was the marked contraction of the upper lip. It was so flat and tense that it was almost impossible to fill it out. If the child was taken at an age of 3 or 4 years and the lip was stretched and kept stretched by the putting in of a simple mass of vulcanite, it was really extraordinary how "adaptive shortening" could be prevented. The result was that when the child reached the age of 13 or 14, and the time arrived to put in an obturator, one had then to deal with a flexible lip which could be stretched out quite easily and so attain a more artistic result. With regard to the cases of restoration of the maxilla, he quite agreed with the remarks of Mr. Lloyd Williams: the point to bear in mind was not to have the slightest pressure upon the tissues. He was always extremely nervous in such restoration cases of getting recurrence from pressure, and he adopted very rigidly the rule laid down by Mr. Berwick, of making the obturator in such a way that at the greatest amount of extension there was not the slightest pressure. He also agreed with the remarks of Mr. Lloyd Williams in regard to the restoration of the mandible.

Mr. DOUGLAS GABELL said that while he was at Manchester he was shown the following very ingenious way of obtaining an impression of a cleft without inconvenience to the patient, invented, he believed, by Mr. Simms: An ordinary plate was employed, at the end of which four small copper wires were soldered, two on each side one above the other, corresponding to the commencement of the cleft up by the hard part. The plate was then put into the mouth and the copper wires bent to lie along, one just below and one just above, the edge of the cleft on either side. When the wires were properly adjusted to the correct level sheets of wax were fitted over them, and in that way a box was constructed which exactly fitted the cleft without submitting the patient to the very awkward operation of having an impression taken so far back, or of having these very movable parts disturbed while the impression was being taken. With regard to the question of the shape of the box when it was

placed in the cleft, it had to be remembered that the movements in the soft palate were not always regular; if cases of cleft palate were carefully examined it would be found that the movements of the two little pieces which were left varied very considerably in different cases. In the majority of cases they moved inwards and outwards, and there were other cases in which they moved upwards and backwards. There was very marked variation in the movements which occurred in the soft palate. He desired to call attention to what he thought he must call the great amount of ignorance which existed in regard to what was the exact function of the soft palate and how it acted in normal cases. A great many authors stated quite definitely that during speaking the soft palate was raised and cut off the connexion from the mouth to the nose. He did not believe that that was so in many cases. The nature of the voice which was produced depended a great deal on the shape of the lower surface of the curve of the palate. It was part of the training of a singer or speaker to know how to control the muscles of the soft palate and to shape the soft palate and so place the tongue as to get a proper opening for speaking through. He thought if more attention was paid to the inferior surface of the obturator instead of the back and side and top portions, better results in speaking would be obtained. He had been rather surprised to hear Mr. Berwick advocate box obturators. He thought they were out of date. Mr. Berwick's objection to the thinner obturators, which were now being made, was that they accumulated mucus on the upper surface. If the lower surface was made concave towards the tongue, with a quite thin obturator the top surface could be made as self-cleansing as a large box obturator; and if the lower surface was made with ample doming, he did not think Mr. Berwick would have the trouble he complained of, of the tongue rising and pushing up the bottom part of the obturator and displacing it downwards in front; he would be able to get his obturator to keep in with a fewer number of clasps. The question whether or not obturators should be made absolutely to fill the gap should depend, he thought, very much on the movements of the parts of the soft palate that remained, and also on the skill of the patient in learning new movements. As far as he could see from looking at the patients, they made great attempts to close the gap themselves during deglutition and also during speech by means of their superior constrictor, because the palate muscles were entirely atrophied. If such patients were fitted with an obturator of sufficient breadth so as not to fill the gap entirely, but so that they could close on to it, he thought with a little perseverance they would be able to use them, that an ample passage between the nose and mouth for ordinary breathing would still be available, and that much better results would follow. It seemed to him by the present arrangement that the passage was being blocked up, which would force the patients to become mouth-breathers, because the space left at the back of an obturator between the posterior wall and the pharynx and the box was not a very considerable one. One had to be very careful in dealing with such cases. If the patient's head was thrown back in order that an impression could be taken and then the box obturator inserted, if the patient bent the head forward, as in feeding, it would often be found that the posterior margin was so tilted back that ulceration was produced.



In teaching patients to learn the use of an obturator it was a useful plan to adopt to ask the patient to practise in front of a mirror so that he could see what movements he was making at the back of the soft palate, and to advise him that if he saw he was making a good movement to repeat it and if he was making a bad movement to improve it. He had experienced the trouble in the case of restoration of the upper jaw of the saliva being driven up into the nose, and had dealt with it by making a special duct down into the mouth to allow the saliva to escape downwards. With regard to the case of the restoration of noses, one which he had had to deal with was that of a girl who had lost her nose. No photograph was available, but the patient very much resembled her mother, and as her mother still had a nose an impression of her nose was taken, from which a model was made for the girl, with happy results. Twice he had attempted a porcelain nose, once with low-fusing jeweller's enamel on a thin copper base, but the sides were so steep that the enamel ran into streaks when fused; and the second was of high-fusing porcelain without any metal base at all, and as it was very thin the red enamel was put on the inside and showed through in a very natural manner, but the nose was very fragile and got broken so often that it was discarded. Both were made at the Royal Dental Hospital.

Mr. BERWICK, in reply, said he had not referred to any cases of the mandible for the reason that he did not want to inflict too long a paper upon the members. There were, however, several cases in which the restoration of the mandible had been attempted to which he could have referred. In reply to Mr. Lloyd Williams, he had said he never troubled to obtain the impression of the cleft; he only took the hard part, for the obvious reason that he was only concerned about the denture. With regard to the modelling of the cleft, he preferred composition, because it seemed to him more plastic than wax. With regard to the question of the method of building up the dome of the obturator, he had not found much difference in the height. All he had paid regard to in the height had been the amount of elevation of the soft tissue, making it sufficiently high to accommodate the impediment of the sides. He had not gone into the question of the vela. In reply to Mr. Peyton Baly, he fully appreciated that there were other methods of keeping the box hollow. In reply to Mr. W. W. Gabell, with regard to the restoration of the speech, he did not know whether Mr. Gabell had seen the patient who was in the building. That case was very striking evidence of what could be attained. He thought it was a matter of experience as much as anything else. Mr. Douglas Gabell had given a very able disquisition on his methods. He thought he had seen one of Mr. Gabell's cases made with the dome obturator. The advantage of the box obturator was its smooth surface. He had heard patients complain bitterly of the food getting clogged in the hollow part, and of course the hospital class of patients were not very particular about cleanliness. They allowed a film of food to remain, which in course of time became really offensive. If, however, a plain polished obturator of the box type was used, no difficulty was experienced and it could be kept clean by simply rinsing it under the tap.



## Odontological Section.

March 31, 1913.

Mr. P. SIDNEY SPOKES, President of the Section, in the Chair.

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### Misplaced Mandibular Canine.

By F. R. SMYTH, M.R.C.S., L.D.S.

I AM indebted to the kindness of my friend Dr. Hugh Galloway, of High Barnet, for the case which I now show you. The patient, a boy aged 16, came to the doctor complaining of a tender swelling under the



Misplaced mandibular canine.

chin. A few days later the crown of a tooth made its way through the skin, and when seen by me the condition was that shown in the photograph. The greater part of the crown of the tooth, which was obviously a canine, projected through the skin almost vertically downwards, in a position immediately below that usually occupied by the right mandibular canine. Except for some hypoplasia of the enamel the form [of the tooth was normal. Examination of the mouth revealed the fact that both the right lateral incisor and canine were absent from their

normal position in the mandible, as the models show. Incidentally it will be seen from the upper model that the maxilla is much contracted, and the teeth very crowded and irregular. The boy himself was undersized and a mouth-breather.

The history given was that when somewhere between 2 and 3 years of age he received a blow on the chin through falling on some stone steps, and that subsequently to this an opening was present for some considerable time, through which a piece of bone was eventually removed. The cause of the misplacement would therefore appear to be similar to that in the case reported by Mr. C. Truman, referred to in Mr. J. F. Colyer's "Dental Surgery and Pathology," where the presence of a sinus had apparently directed the tooth in its course. This and another case referred to in the same work, recorded by Mr. D. Whittles, are the only similar cases I have been able to find reported.

It will be interesting to hear whether any members present have met with similar conditions.

#### DISCUSSION.

Mr. WILTON THEW mentioned a case, of which he showed a photograph, somewhat similar to Mr. Smyth's. The patient was aged 33. The history was that at the age of 7 his jaw had been broken in the region of the canine. This joined up in the usual way, and apparently no symptoms developed until about four years ago, when he began to have abscesses in the lower left canine region. The man came to the London Hospital, and skiagrams were taken, which showed the crown of the canine tooth, without any root, lying horizontally in the jaw at a considerable depth. From the X-ray picture it seemed impossible to say whether it was the crown of a canine tooth pointing backwards or an inverted molar root pointing forwards. The man was very ill, presumably owing to the extremely septic condition of his jaw, from which pus poured freely. Ultimately an incision was made along the line of the alveolus, and the tooth gouged out with a straight elevator. It proved to be the crown of the canine tooth, had an absorption cavity in it, and showed obvious signs of hypoplasia. The case afterwards went on well. Presumably the developing tooth was smashed when the jaw was broken, and remained more or less stationary.

The PRESIDENT (Mr. P. Sidney Spokes) said he had seen a somewhat similar state of things in a dried specimen, but he did not remember a mandibular canine erupting like Mr. Smyth's did, though he knew such cases had been recorded.

### The Preparation of the Mouth before Operation.

By J. G. TURNER, F.R.C.S., L.D.S.

THE answer to the question, "How to prepare a mouth for operation" may be put briefly, "Clean it, and leave it easily cleansable." To the question "Whose mouth?" the answer is the patient's, the surgeon's, the anæsthetist's, the nurse's, the theatre attendant's, the sick room attendant's, in fact, the mouths of all who will make up the invalid's environment, even of those who later may visit and perhaps kiss him, because that, even in ordinary speaking, it is impossible to prevent the projection of saliva. The reason for cleaning the mouth lies in its inherent septicity. Even from the most cleanly mouth, the mouth streptococcus can always be recovered, while in the less cleanly, pathogenic and putrefactive organisms abound. A septic mouth may allow of direct infection of any wound made in the mouth, nose, throat, air passages, or intestinal canal, and later of parotitis; of infection through a finger to a wounded eye, &c.; of pulmonary infection during anaesthesia or later; of infection through the blood-stream to a wound in any part of the body—and here we must include childbirth.

Circulation of living germs or spores in the blood is probably far more frequent than is usually recognized. Circulation of small numbers such as may account for chronic endocarditis, or of smaller numbers, I conceive to be a common occurrence. Such circulating germs may be caught in the thrombi of the injured vessels, and there given an excellent culture medium. This explanation may be extended to acute epiphysitis, which commonly has a history of previous injury, and emphasizes the danger even of playing games with an unclean mouth.

Swallowing of germs and toxins must be a constant occurrence in a septic animal, and must weigh in the balance against the patient's chances of recovery. Absorption of germs and toxins will take place through any lesion of mucous membrane, however slight. Absorption may be toxic only when the clinical signs are those of chronic overgrowth or of slight catarrh, but in all cases of acute catarrh or of actual lesion germ absorption will also be present. Any clinical manifestation of inflammation from the most chronic to the most acute may be taken as an index of the presence of germs in injurious quantities and

the presence of acute catarrh, or of ulceration, as an index of germ absorption.

It need hardly be pointed out that when there is pus discharge from the tooth sockets, ulceration is present, but I want to insist on the fact that in far less obvious conditions of disease than this there is actual ulceration both of the alveolar bone-margin and of the toothward surface of the gum forming the more or less deepened periodontal sulcus. The cutting of a few microscope sections will prove this point. There is also ulceration under every edge of tartar, under every overlapping filling, under the edge of every ill-fitting crown, cap, or bridge, round every septic root, and an acute catarrh under a large number of tooth-plates. The constant swallowing of putrefaction products, afforded by the overflow from carious teeth or interdental pockets filled with putrefying food débris, or by the exudation from underneath gold caps of the putrefying fluids impregnating the cement used to retain them in place, is a not infrequent cause of persistent vomiting, which may, of course, be a serious danger after operation. I make it a rule to smell every cap I take off (warming it gently makes the smell more obvious), and I find that, with very rare exceptions, the cement used to fix them stinks abominably.

The actual preparation of the mouth may be considered under the following heads:—

- (I) The ideal. Preliminary to operations when there is ample time for preparation.
- (II) Preliminary to operations of urgency.
- (III) Preliminary to dental operations.

#### (I) IDEAL PREPARATION.

The mouth has to be rendered clean and easily cleansable. This cannot be accomplished without ample time. A fortnight will be found none too long in the case of the ordinary septic mouth. Tartar must be thoroughly scaled away, and this cannot be done in one sitting. Probably three successive days will be needed to complete the scaling. All ill-fitting caps, crowns, and bridges must be removed, and I regard as ill-fitting every cap which is thrust up under the gum edge. This procedure will probably necessitate some temporary repair work, and all fillings done now should be of the smallest possible dimensions and as flat as possible to allow of ease of cleansing. This repair work is better done when all scaling is finished, and may occupy another two

or three days. At the same time, all overlapping and rough fillings must be ground flush and polished, all faulty fillings repaired, and the treatment of abscessed teeth begun if such are to be saved. At each sitting the teeth should be thoroughly brushed with circular engine brushes carrying finely powdered pumice, and the interstitial surfaces forcibly rubbed absolutely up to the gum edge. To do this, I use a steel probe, round the end of which a wisp of cotton-wool is wrapped and then dipped in a weak solution of carbolic and citric acids. After three to six days, the mouth will be fit for extraction of septic, incurably abscessed, or loose teeth, and in about a week from that the mouth should be comfortable enough to allow of an operation being undertaken. Extraction of upper teeth not infrequently discloses chronic antral disease or abscess, both unsuspected. Extraction should be done under a general anæsthetic to limit the chances of a septic socket, an accident which more frequently follows the use of local anæsthesia.

Hitherto I have not mentioned the word pyorrhœa. The fortnight I have asked for above is chosen as being the time in which I find by experience an average case of pyorrhœa alveolaris can be brought to a reasonable state of cleanliness, and the treatment above outlined is part of the necessary treatment of the condition. In addition, however, to scaling and thorough cleaning of the teeth, uncleanable pockets may need to be destroyed by excision of portions of the gum, and at least a week must be allowed for healing of the last of these wounds. During this preparation artificial dentures, especially partial dentures, which of necessity cause stagnation round the natural teeth, are to be worn only at meal-times. This ideal method follows the old maxim, *festina lente*, and subjects the patient to no risk or strain.

You will notice I have said nothing about mouth-washes. You can, of course, do no harm with mouth-washes, but the amount of good they can do is but superficial and therefore very limited. They cannot penetrate beneath the layer of mucus which coats everything in the mouth, and they cannot get beneath tartar edges or into pyorrhœa pockets. From experience I have learned that mechanical cleansing of the teeth is far the best method of attaining mouth cleanliness, and I use citric acid for its cleansing properties to assist vigorous rubbing.

Vaccines are sometimes recommended, more especially in extensive dental and other mouth operations, as a prophylactic measure. If care be taken with preliminary cleansing, I believe this to be quite an unnecessary precaution, and perhaps it is not quite free from risk. I have never employed it myself, and I have carried out my own procedure

successfully in cases where preliminary use of vaccines has been urged as imperative.

Difficult extractions had better not be undertaken shortly before a general operation, since the injury done to the bone in extraction usually leaves a painful osteitis and perhaps necrosis. This refers chiefly to impacted third molars. The tooth should be brought to a state fitting it for extraction and kept so during convalescence.

#### (II) PRELIMINARY TO OPERATIONS OF URGENCY.

When the operation is urgent and time is not available tartar and loose teeth should, if possible, be removed and all pockets and interdental spaces cleaned out with steel probe and cotton-wool dipped in either citric and carbolic acid lotion, or bicarbonate of soda and carbolic acid lotion. When nothing else can be done the teeth and mouth should be well rubbed and sponged with one of the above solutions, followed by prolonged use of a mouth-wash of carbolic acid (1—60) immediately before operation. If possible, half an hour should be spent on this cleaning. A whole mouthful of septic teeth may be safely removed if the patient have immediately before operation spent half an hour in having his teeth scaled and rubbed with sod. bicarb. 10 gr. to 1 oz. carbolic lotion (1—60) and gargling his mouth with the same lotion, a proceeding which is more often possible in such operations than in the case of general operations of urgency.

The success of this procedure is in great measure due to the fact that extraction removes all sources of sepsis, and is contingent on the absence of difficult extractions and avoidance of thrusting the forceps blades far up into the bone or tooth-sockets.

#### (III) PRELIMINARY TO DENTAL OPERATIONS.

Ideal cleansing preliminary to dental extraction should of course extend to the whole mouth, but in practice in the case of extraction of a single tooth presenting no special difficulty, when a local anæsthetic is not used, careful cleansing of the tooth and its two neighbours, and the use of a mouth-wash immediately before operation, will be found sufficient in a fairly clean mouth. The teeth must be specially cleaned at the necks under the gum edge, especially the tooth to be extracted, since germs left in this situation will be thrust up into the bone or socket by the blades of the advancing forceps, particularly when

operating by displacement. When a local anæsthetic is used, since there will be no bleeding and no blood-clot to keep the part aseptic, the whole mouth must be carefully cleaned.

The preparation for extensive extractions I have sufficiently indicated under the first two heads. Of course, when the teeth are to be extracted, fillings need not be polished smooth nor crowns necessarily taken off, but tartar must be removed, especially where it is likely to flake away, and care must be taken to clean under every edge of filling, crown, or interstitial tartar.

In the case of septic or suppurating impacted teeth, the part should, if possible, be laid open, syringed, and packed till clean before operating. This limits the chance of subsequent bone trouble.

I want to draw special attention, as I have done before, to the danger of administering anæsthetics to patients with septic mouths.

Obviously there must be differences in treatment according to circumstances. The financial position of the patient and the seat of the operation must influence considerably the question of extraction. In hospital practice teeth must necessarily be sacrificed in far larger numbers than in private, and in operations such as those for cancer of the tongue or on the air-passages the very limit of dental asepsis must be aimed at. This often means extraction of every tooth, whatever the position of the patient, and to avoid the danger of septic complications involved in the use of local injection anæsthesia, general anæsthesia should be employed if possible.

#### DISCUSSION.

The PRESIDENT (Mr. P. Sidney Spokes) said the paper presented several eminently discussible points, though probably most of the members would agree with the general principles which Mr. Turner had laid down. He was relieved to find the subject presented in such a moderate way. He had prepared himself for hearing more sweeping statements, and more drastic operations recommended for the mouth. Though all were at one in removing teeth which might be a cause of sepsis otherwise incurable, there were some who feared that the pendulum had recently swung in the direction of too free removal, and that not sufficient consideration was given to saving teeth when that was possible. The profession might almost be divided into two schools: those who believed in making a clean sweep of the teeth on the slightest provocation, and those who believed in retaining the teeth in the mouth, provided they could be maintained in a reasonably healthy state. There were also some points in the paper in regard to the form of anæsthetic, which members might like to take up.



Mr. STANLEY P. MUMMERY said he wished to deal only with Mr. Turner's remarks concerning local anaesthesia for mouth operations. He had now been using local anaesthesia for over four years. He removed two out of every three teeth in that way, and his experience led him absolutely to deny Mr. Turner's statement that sepsis was more liable to follow when local anaesthesia had been employed. His distinct impression was that the reverse was the truth. When using local anaesthesia, one could prepare the patient beforehand by rinsing out the mouth, and painting the part with iodine and whatever else one wished, and immediately after the extraction the patient could wash the mouth out again, and an atomizer could be used on the sockets. Unless sepsis were injected into the mouth with the syringe—a totally inexcusable accident—he saw no reason for Mr. Turner's statement that local anaesthesia was more often followed by sepsis than was general anaesthesia. It might be urged that local anaesthesia reduced the vitality of the part, but he did not think such was the case; the injection of a few drops of fluid could not produce any mechanical damage, and there was nothing in either novocain or other drugs used to cause chemical harm.

Mr. J. F. COLYER said he would like to reply to Mr. Mummery's statement by saying that his experience of local anaesthetics was that there was a greater chance of the tooth sockets becoming septic after their use. One had only to look at a tooth after using them to see that there was no formation of blood-clot, which was Nature's first line of defence against sepsis. He quite agreed with what Mr. Turner said about preparing the mouth; if only one could always carry it out! Those engaged in hospital work knew the practical difficulties owing to the large number of patients requiring treatment, and the neglect of patients to carry out instructions. For years he had tried to insist on every patient having a mouth-wash after extraction of teeth, but he was informed that only about one in five applied at the dispensary for it. During the last six months he had carried out the practice of swabbing mouths all round with a 2 per cent. solution of iodine in alcohol; and his after-results had been excellent. He could not altogether agree with the remark of the President about saving teeth. As a practitioner, he did not believe he had any right to leave in his patient's mouth a potential source of disease, and when he had a patient with septic teeth, associated with malignant disease about the mouth, he strove to leave no tooth there which could be a source of sepsis. If he had patients with chronic superficial glossitis in the regressive stage, he took out every doubtful tooth, because he knew that a source of sepsis being left behind would increase the liability of the patient to develop epithelioma of the tongue.

Mr. GORDON R. SHIACH said that although he considered the question of the anaesthetic a little aside from the main subject, he would support the remarks of Mr. Mummery. For about ten years he had used local anaesthetics almost exclusively. With regard to the occurrence of endocarditis, the only case of endocarditis he knew of in his own practice was where the anaesthetic

was chloroform. He believed Mr. Reeve would support him in saying that, with proper precautions against sepsis, there was little or no trouble with local anæsthesia in the large majority of cases, and he regarded Mr. Colyer's objections as purely theoretical—i.e., for adults. In the case of children he gave in at once.

Mr. PITTS said that most surgeons realized that where operations were to be performed on the mouth or adjacent parts some attempt should be made to cleanse the teeth and gums, though unfortunately they did not always give the dentist sufficient time for the purpose. But with regard to operation on other parts, he thought that a full recognition of the desirability of a clean mouth was still lacking. It had always seemed to him that the respiratory complications which sometimes followed the prolonged administration of an anæsthetic might, in part, be due to a condition of oral sepsis. When one remembered how often ether was given by the closed method, in which the patient went on breathing and re-breathing into the bag, one could well imagine how extremely foul the vapour in the bag would become in cases of oral sepsis, and that the germ-laden gases passing into the lungs might easily cause infection. With regard to local anæsthetics, he agreed with Mr. Turner that the subsequent healing was usually retarded. He only used that method in patients whose gums and periodontal membranes were quite healthy; but even then, and taking all precautions to render gums sterile and the needle and solution aseptic, he found that generally the healing of the socket was not so rapid as in cases where no local anæsthetic was used.

Mr. WHITEHOUSE suggested that where it was necessary to perform a considerable number of extractions it was better to do all those in the maxilla first, and then all in the mandible at a subsequent sitting. The practice of operating on one side only, because it enabled the patient to use the side that was intact, might induce septic sockets in the mandible from the gravitation of sepsis from the maxilla.

Mr. D. GABELL expressed his agreement with Mr. Turner's remarks on the preparation of the mouth, but there remained the practical question of how it should be done. Mr. Turner said one should remove all the tartar, as if that were an operation which did not of itself involve great risk of sepsis. In his early efforts to remove tartar completely he was somewhat enthusiastic, and made many wounds in the gum in consequence, so that he found some of his patients neglected to keep a subsequent appointment, because they were said to be laid up with "rheumatism," and he did not doubt that the ailment was of his causing. The removal of the tartar required great nicety, and the avoidance of wounds. At the Royal Dental Hospital an attempt was made to get students to take more care with the mouths of patients in the gas-room before extractions were done. The dressers were instructed to cleanse the mouths of their patients before extracting, and, from what he saw of the mouth condition an hour or so later, there seemed more risk from the scaling than from the main operation for which the patients attended. He considered a mouth-wash was of service in

keeping the mouth in condition ; perhaps it was of more use mechanically than chemically, but if used frequently it was of definite benefit. He asked his patients to use a weak solution of Condy's fluid often, instead of a strong solution less often. Mr. Turner said the layer of mucus would protect the germs from injury by means of the mouth-wash ; but he (the speaker) considered that if one could taste the disinfectant it was an evidence that it had penetrated some depth into the tissues. The astringent effect of the mouth-wash he regarded as of equal importance to the antiseptic effect ; it relieved the swellings and permitted of better drainage. He did not like the popular spraying apparatus, as it blew much impurity from the region of the wound into a spray that was inhaled by the patient, and probably led to many germs getting into the bronchi instead of being allowed to rest between the teeth. He preferred to use a flow of water through a blunt hypodermic needle, which he could gently insert into the pockets and wash out from below. If pockets were left, there was danger of their being filled with more germs ; therefore he injected paraffin, with 1 in 500 perchloride of mercury to render it aseptic, to fill them temporarily. It took several hours for that ointment to make its way out, and it lubricated the rough pieces which were bound to be left after the operation of scaling. After this treatment he found the gums did not suffer so much. On the question of a local anæsthetic he agreed with the remarks of Mr. Turner. The worst wounds he had seen after extractions had been those where a local anæsthetic had been used, and they had been very ugly wounds. He did not think it was possible to inject fluid into a socket which had inflammation about it, and pockets of pus, without running a risk of driving this pus deeper into the tissues, and no superficial mouth-wash, or cleansing, or rubbing would be of any use to remove those foci of inflammation. He had found iodine very useful in cleansing the mouth. His custom was, almost at the commencement of the operation, to paint the teeth, as neatly as he could without it going on to the gum, with liquor iodidi fortis, because that gave him a valuable indication of how much dirt there was on the tooth. Teeth might look clean in the ordinary way, but when painted with iodine and the mouth rinsed out dark brown markings would be seen, and these helped one to detect and remove the worst areas of infection. The markings also showed the patient that he had not been cleansing the mouth enough, a statement he was inclined to resent, unless it were proved to him.

Mr. T. STORDY remarked that several speakers had mentioned the use of a mouth-wash, but had not said what the temperature of it should be when used, a point which he regarded as of some importance. Many members must have had the experience of prescribing a mouth-wash for use after extractions, and the patient coming back with the mouth obviously septic. Inquiry showed that most of those patients had used the wash either cold or tepid. He considered it should be used at quite blood heat. If such cases were treated with a hot wash, there was improvement in a couple of days. The treatment required was on a par with that of the nasal cavity, and no one dreamed of using a cold nasal douche after operative measures, for it lowered the vitality of the tissues and rendered them more liable to infection.

Mr. A. E. BAKER, remarking on the statement by Mr. Turner that the gums were bloodless after local anæsthesia, said he obviated that by asking the patient to suck hard after the extraction had been carried out. That restored the blood flow, and it filled the socket and promoted the formation of a healthy clot. Hence the gum healed more readily and there was less risk of septicity.

Mr. TURNER replied that the discussion had, to a great extent, answered itself. Perhaps if the President divided practitioners into two classes—those who did extractions too much, and secondly the others—he (Mr. Turner) might be permitted to retort by saying that the two classes were those who saw a good deal and those who saw less. He was sure the extractions he performed were done because dangerous sepsis was present, which was demonstrable, and would be admitted were it but seen by the President's second class. With regard to the employment of local anæsthesia, there was no getting away from the possibility of damaging the tissues both by pressure and by keeping away the normal blood too long by local anæsthesia, and by some form of cytotoxicity which possibly occurred unless an isotonic solution was employed, and one could not be sure of the damage one might do to the reparative cells of the part. The fibrous tissue might not be injured, but the delicate cells were readily injured. The sockets certainly remained unfilled with blood after local anæsthesia, and he thought Mr. Baker's suggestion of telling the patient to suck the gums was a good one. Others resorted to puncturing and scaring until blood filled the sockets again. But in spite of these expedients his experience was that with local anæsthesia there was greater liability to septic troubles, or at least inflammatory ones, so that there was retardation of healing. Therefore, whenever possible in the class of cases under consideration he preferred a general anæsthetic. As the question under discussion was the preparation of the mouth for operation, he did not know whether the subject of how many teeth should be removed at a time could properly be included. But having once got the mouth clean, if it was not a question of too much shock, or making the patient uncomfortable, it was, in his view, better to get rid of the whole lot quickly. But in general it would be found that people were afraid of the shock and reasonably anxious as to the discomfort after removal of the teeth. In the removal of tartar one could not avoid injuring the gum, but if the mouth were kept constantly washed out no harm resulted. He was not aware of the special value of the mouth-wash used warm; he was in the habit of looking for immediate improvement on the first day after cleaning up the teeth, and on the second day there should be further improvement.

**James Gordon of Bristol: An Echo from the Past.**

By GORDON R. SHIACH, L.D.S.

THE subject of my sketch (fig. 1) was born in Nairn, "the Brighton of the North," in the year 1795, being the son of William Gordon, known in his time as the Poet of Nairn, who in turn was the son of another Gordon, a Forres man, of similar literary talent. I have mentioned the literary tastes of James Gordon's father and grandfather as an indication of the source of his inherited culture, and I could tell many a story of this old man, showing the imaginative nature to which James Gordon fell heir. This William Gordon must have been in many ways a man of strong individuality, for in addition to the volumes of poems he left behind him, the story of his attempts at aviation in the eighteenth century, detached as he was from the influence of the mechanical science of his day, mark him as a man of resource as well as imagination. He constructed something in the way of a flying machine, and made an attempt in public to fly from Bunker's Hill on the links of Nairn. No matter that the attempt was a failure and that Gordon broke both legs in his efforts, it was surely a proof that there was something in his ideas, that he had succeeded in getting so far off the earth as to bring about the final disaster. I have seen a half-length portrait of him in oils, depicting a distinctly pinched and withered old man with the bright eye of a child, and an expression of keen activity, a reflection of the soul which must have burned within him to the last day of his life of 96 years.

From such a parent did James Gordon spring, and little wonder is it that his record was a good one. One of a family of seven and educated in Nairn, he went to Inverness to learn watch-making with William Keith (a trade name to conjure with in his time), who was later to receive him as a son-in-law. While still a youth newly through his apprenticeship he migrated to Bristol in search of work. While there on the outlook for work, to occupy his spare time he made a watch, a fact which was mentioned by a young man in the same lodging to a dentist friend, who, in doubt as to the truth of the watch story, requested an interview with this extraordinary lad. This dentist, incredulous at first, was so struck with the lad's ability that he said he was losing his time and persuaded him to go in for dentistry. The name of this practitioner has been lost, but to him must be given the credit of taking James Gordon by the hand and supporting him while he learned the

profession as then practised, about 1815, or shortly after. Later on Gordon began practice for himself in Park Street, then a quiet residential street between Clifton and Bristol. He continued in this practice until past middle life, and in 1852 (the year succeeding the first exhibition in London) he married Catherine St. Clair Keith, a daughter of his old master, a lady twenty years his junior, and whom he had nursed as a small child in Inverness. Shortly after his marriage he retired from active service and took up his residence in Inverness, afterwards changing to Nairn, where he died at Bristol Cottage in 1864, in his seventieth year, survived by his widow and a son and daughter.



FIG. 1

James Gordon, dentist in Bristol, 1795-1864.

James Gordon surely chose a mate to complete his nature in every respect, for as I can recollect her she made one think of stories of a century before her time, breathing an air of refinement in physical and mental capacity, which impressed itself upon my boyish mind in a way never to be forgotten. Her musical talent competed with her skill in miniature painting and such art, and specimens of the latter are justly treasured as a legacy of which any professional artist might feel proud. One might speak of at least four generations of these Gordons in which poetic and musical talent and skill in handiwork were outstanding features, William Gordon being the last, surely a strong argument in

favour of heredity being an element in the formation of our mental as well as our physical constitution.

While carrying on a lucrative practice James Gordon, like many another genius, allowed his fancies to interfere with his mundane interests, but these hobbies had such a bearing upon his professional development that I feel they are worth recording. One must remember



FIG. 2.

Anatomical figure constructed from ivory, the muscular system being capable of dissection down to the skeleton, as clearly shown in left lower extremity.

that Mr. Gordon lived in the age of natural teeth and bone, or at best the old forms of French porcelain teeth and gold plates, so that the original carvings, to which his spare time was devoted, were more or less expressions of the skill which he had acquired in his profession. I said his spare time was so occupied, but in that I was not quite correct, for my father has told me how common an occurrence it was for



Mr. Gordon to take a denture to his workroom for alteration, and set it aside to carry out some sudden inspiration in another line, forgetting meantime that he had a patient, more or less impatient, upstairs.

The largest piece of work James Gordon ever undertook was the construction of a complete anatomical figure (fig. 2), which in the family circle was known as "Ghastly Sam." The inspiration arose thus: Gordon took part in a discussion with other dental surgeons, and I



FIG. 3.

The heart and lungs.

suppose medical practitioners also, upon the period of the development of the primary dentition. He took up a distinct attitude, and to prove his theory constructed a child's head in ivory. This piece of work is now, I believe, in a Bristol museum. A local paper took up the matter, and dwelt, not upon the merits of the discussion, but upon the anatomical knowledge and mechanical skill of the artist. Gordon was a man of retiring and modest nature, and in his quiet way rather laughed at the fuss made over his small effort, saying that he could easily, given time,

complete the whole body in a similar manner. The idea so originated developed into "Ghastly Sam" as you now see him. After twenty years' labour he was completed in time for the 1851 exhibition, and shown along with other two specimens of Mr. Gordon's work, a carved wooden vase coloured to imitate bronze, and a carved wooden figure representing Blind Belisarius, a sixth-century Roman general who was reduced to beg his bread in the streets of Constantinople after having been one of the most successful generals of his time, and an ornament to the reign of Justinian, who rewarded his devotion by blinding him, so at least later history says. For this Mr. Gordon received a bronze

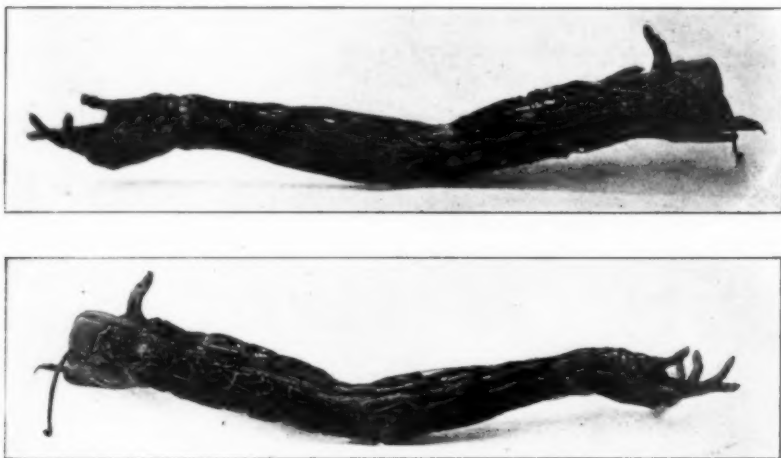


FIG. 4.

Right upper extremity, showing nerves and blood-vessels, both superficial and deep, carved entirely from ivory.

medal as well as the Exhibitor's medal, and it was no small honour to have one specimen of a man's work accepted, for the Exhibition Committee then were most exacting, receiving nothing of small merit, and nothing in any sense a copy.

To return to the principal figure, it is supplemented by a separate model of the heart and lungs (fig. 3). The former is of ivory, beautifully wrought and coloured, and so constructed that it can be opened up to show the valves, &c., of the interior. Each vessel is lettered with a reference in his description book. The lungs are formed of ivory,

seaweed, and gold-beaters' skin, while the trachea is of ivory and a bird's foot. There is also a separate model of the arm (fig. 4) showing the blood supply and nerves, which I have attempted to reproduce on the lantern slide. The supplementary model of the brain is also of ivory, and is made in various vertical and transverse sections. I believe that the principal viscera were duplicated in ivory, and that there was a model of the leg made on similar lines to that of the arm, but these I have been unable to procure. The main figure, on a scale according



FIG. 5.

"The dentist" (carved from wood and ivory).

to the maker of  $5\frac{1}{2}$  in. to the foot, shows in detail the muscular system principally, while as many other features are included as the unyielding material would admit. The head shows a different dissection on each side; the skull can be opened and the brain removed, showing the main features of the base of both the brain and the skull. The left eye can be removed, and shows the arrangement of the muscles, &c. I need not, however, describe further, as the members will have an opportunity

afterwards of seeing the method and extent to which the dissection of the muscular system has been carried.

Another piece of Gordon's work which I have often seen and admired is a complete set of chessmen carved in ivory. The reds and the whites are different in design, while all the pawns show a different head in profile, an expression of the genius of the man, one of whose maxims was to avoid slavish copying.

Other subjects which I have had the privilege of seeing are a series of busts of Shakespeare, Dante, &c., besides various small fancies, which expressed the passing idea of a day. A piece of work belonging to his days of retirement, when well into the sixties, was an ivory model of a castle surmounted by a clock tower and embellished by historical figures, one of which I have beside me. It was never quite completed, and like many another on a larger scale has been allowed to fall into ruin. When his powers were beginning to fail he took his little daughter on his knee and asked her what her greatest desire was, the reply being, "A school of dollies." This he began, the house, school-room, benches, and some of the figures being constructed in ivory, but the entire work was destined never to be completed. I here show you photographs of two of his efforts which I possess, but which I have not taken with me. The first is that of a dentist in the act of extracting a tooth (fig. 5), and is most expressive, although some portions are somewhat broken. The main figures are carved from wood and coloured, while the heads and hands are of ivory. The expression of wickedness on the operator's face and of agony on the part of the patient are most amusing, while the chair and costumes of the period are interestingly reproduced. The other subject is the historical one of Hector calling down the blessing of the gods upon Andromache and her son, one of the most admired passages of the "Iliad" (fig. 6).

These were the days when the dentist at the bench was, according to Mr. Bowman Macleod, already quoted, "a horny handed son of toil." Certainly the working material was hard enough, and even with perfectly adjusted hand tools there must have been hardness of the operator's palmar surfaces, difficult to deal with in unison with the lighter touch necessary for many features of the work. In addition to his other talents, James Gordon could draw with both freedom and precision, although his sense of colour was not so good. A complete list of the works of his pastime would only weary you, but I cannot refrain from referring to a large case of stuffed birds, the study of which used to delight me as a child. I was never tired of hearing how one specimen

was procured, where another came from, how the skeleton of a mouse was prepared by the industry of ants; and, although it does not comply with our ideas of the æsthetic, still it shows his expression of individual artistic treatment of a subject which had its admirers in a past generation. Gordon had the poetic gift of his family, and I think I have only to read to you the closing sentence of his description of the anatomy of



FIG. 6.

"Hector and Andromache" (modelled in wax).

the human ear to have your admission that he could express himself in prose:—

"The functions of this organ, and the advantages and pleasures of this Sense, would furnish ample materials for a work on this subject alone. Man finds the greatest pleasure and advantage in hearing and comparing his ideas with those of his fellow-men; his own ideas are thereby modified, rejected, or established in his mind. The fund of human knowledge is thereby ever accumulating through the intercourse of mind with mind. The Sense of

hearing is the principal medium through which we interchange our intellectual conceptions, and from it we at once find advantage and social delight, resulting from the communication between the ear and mind."

One may ask wherein lies the present-day interest in such a reminiscence. I claim that it is well for us in these days, when we are tempted to fancy that we have risen to heights never dreamed of by the men of a century ago, to remember that there were giants in the past, and that though in details we have surpassed their efforts in conservative dentistry, still we have built, and are now building, upon the foundations so skilfully laid by a past generation. Whatever line the progress of the next fifty years may take, doubtless the changes will be as great as the last fifty years have shown, and let us hope that our grandsons may respect our professional efforts as we can those of the James Gordons. I have said nothing about the actual professional work of my subject, because all I know is that he was a successful practitioner, and I think we are safe in concluding, from an inspection of his hobbies, that he was an ornament to his profession. His detailed knowledge of anatomy is significant of the possibilities of education in Bristol, even in those days, when our profession had not the recognition which it has since achieved, and which it is still striving to increase. I do not wish to open up the question of the comparative advantages of the full medical and the purely dental qualifications, but I must remark that in this review of Gordon's life we have an indication of how a man's everyday work can be turned into a fascinating hobby through the advantage given by a generous education and a wide knowledge of the outer fringes of his profession. Such being the possibility, and in this case the actual fact, not only may the drudgery of practice be lightened, but the work of the individual is likely to be thereby improved and stimulus given to greater effort, and the profession at large has a chance of being benefited by some addition to its store of accepted fact.

Mr. COLYER exhibited a miniature skull, carved in ivory, the work of Mr. Gordon, which was in the Odontological Collection of the Royal College of Surgeons for some time.

Mr. SHIACH remarked that this was undoubtedly the specimen which he thought was still at Bristol.

## Odontological Section.

April 28, 1913.

Mr. P. SIDNEY SPOKES, President of the Section, in the Chair.

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### The Cure of Mouth-breathing.

By W. W. JAMES, F.R.C.S., L.D.S.

THE ill-effects produced by nasal obstruction and mouth-breathing are so significant that in all branches of medical science the establishment of normal respiration is regarded as of the utmost importance. At the present time the procedure for the establishment of nasal respiration consists of operative measures followed by breathing exercises and, of course, voluntary effort by the patient. In many cases this may suffice, but in a large number mouth-breathing continues. The majority of failures are due to the persistence of a habit which, although controlled during the day, recurs at night when voluntary effort is impossible.

Those of us who are responsible for the care of the mouth have little difficulty in detecting a mouth-breather. The effect on the mucous membrane in the front part of the mouth is characteristic; in children gingivitis is present where the tissues are exposed to the air, later pyorrhœa alveolaris becomes established as is seen in adults who are mouth-breathers. Imperfect development and deformity of the bone of the face is well known in mouth-breathers; the maxillæ are chiefly affected, one of the most frequent characteristics being protrusion of the incisor teeth.

The difficulty of dealing with patients who were able to breathe through the nose, but whose mouths clearly indicated that they continued to breathe through the mouth, led me to attempt breaking the



habit of mouth-breathing at night which was the cause of the trouble. For a considerable time I used strips of strapping which were placed across the mouth, the position of the strapping being varied from night to night. In one or two cases bandaging was also used. This method was successful in many cases, although trying and irksome to the patient. The apparatus about to be shown was tried and has been used in a number of cases; the success in the majority of instances has been so marked that it seemed to be of sufficient interest to bring it to your notice.

The apparatus consists of a wire frame, over which thin sheet rubber (dental rubber-dam) is stretched; it is placed inside the lips and cheeks, resting upon the outer surfaces of the teeth and gums. The frame is

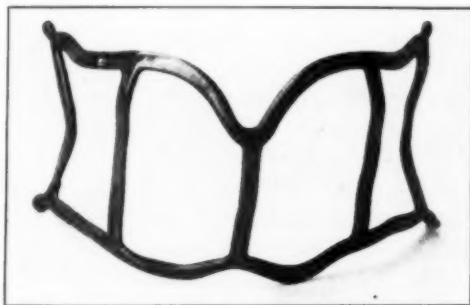


FIG. 1.

Frame of apparatus to prevent mouth-breathing.

made to a model. An impression is taken in composition, which should not be made too soft, as a sharp impression is not required. It is better not to use a special tray except for small children, when the taking of the impression may have to be carried out quickly; a tray would have to be so uncomfortably large for the patient in order to obtain a satisfactory impression; in children one may have to be satisfied with what one can get.

The following method is given in detail, as an accurate model is essential for success. The teeth are occluded, the impression composition is rolled into a sausage-like shape and is inserted inside the lips and cheeks, it is then pressed against the teeth and upwards and downwards into the sulci; the lips are closed over the impression material. The operator standing behind the patient places a hand upon each

cheek with the fingers over the lips; uniform pressure is made over the impression material. Cold water is then syringed inside the cheeks until the composition is quite hard; the water is allowed to escape into a bowl, the head being tipped forwards. The removal of the composition may cause the ends to be bent inwards; this is the reason why a special tray may be necessary in children. The impression should extend as far back as the first molars and to the full depth of the sulcus of each jaw. The composition can be replaced after being hardened in cold water if there be any doubt of its accuracy; on this account too sharp an impression is undesirable. The model is poured, a zinc cast

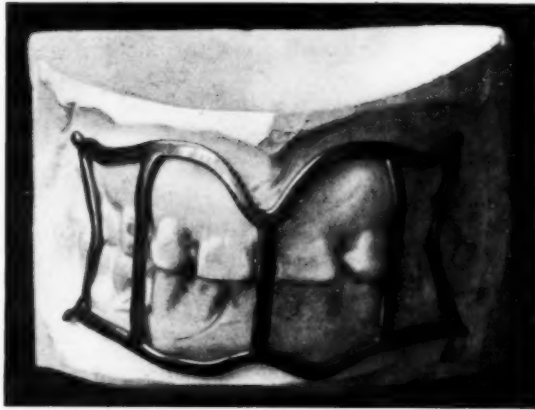


FIG. 2.

Frame in position on model. (The downward bend for the frænum can with advantage be carried lower.)

and a lead die prepared. The shape of the frame is marked out on the model; the outer wires are fitted, soldered, and struck, the vertical supporting wires (usually three in number) are also fitted, but soldered at one end only, the other end being slightly longer than is required, it is then struck; finally, the other ends of the wires are soldered and the whole frame struck up. The exact shape of the apparatus and the position of the wires are shown in the illustrations. The upper horizontal wire is placed near the top of the sulcus, but slightly lower at the ends, in the middle line a depression corresponding with the frænum labii must be made. The frame is chiefly supported by resting upon

the projecting teeth and alveolar mucous membrane of the maxillæ. The lower horizontal wire should not be carried to the lowest part of the sulcus, for although it should fit it cannot do more than rest against the tissues of the mandible as they are more or less vertical.

The chief discomfort is from rubbing; this is prevented by making the frame large enough to be steady and by avoiding bony eminences, the horizontal wires being carried either above or below them. The frame should reach almost as far back as the first molars and the horizontal wires approximate slightly to one another, in order to allow the angles to have rounded projections over which the rubber can be stretched. On no account should the frame extend beyond the area of accurate impression, as otherwise the tissues are almost certain to be rubbed. The frame should be large, chiefly to keep it steady when worn, but also to prevent displacement from the mouth, which can easily occur if the apparatus is small.

The wire used in most cases has been German silver, gilded after completion. Fine wire makes a lighter frame, which is less noticed, but it is very easily bent and is then uncomfortable. Dental alloy wire has been used, also gold. An attempt to make a vulcanite apparatus was not successful, as the parts were so easily chafed by it. At present the size of wire used is thicker than formerly. The wire was drawn down between rollers in order to give an oval contour; a draw plate would probably be better for this purpose. When used the rubber is stretched over the frame and the surplus trimmed off with scissors. A supply of rubber is given to the patient, who has directions to change it frequently. If the rubber is stretched too tightly it is apt to tear and may press upon the teeth, causing them to become tender.

The apparatus may be worn during the day if it is thought desirable, as in one of my patients who was a thumb-sucker no rubber was put on during the day, but the frame alone effected the purpose of preventing the thumb being inserted. Ordinarily the apparatus should be used at night as has been stated. When the apparatus is in position mouth-breathing is absolutely impossible and the patient is compelled to use the nose for respiration.

The patient may find it impossible to use the apparatus if nasal obstruction exists, in which case a surgeon should be consulted. Some discomfort is usually felt for one or two nights and then the inconvenience should be very slight; several patients were able to sleep comfortably on the first night. The comfort of keeping the mouth

and throat moist made so great a difference to some individuals that they slept better, and in consequence prefer to have the apparatus. One patient says he is so attached to his that he can hardly sleep without it; he suffered from a chronic sore throat which has improved in a remarkable manner. Besides improvement in the condition of the mouth and throat, the nose also benefits; chronic nasal catarrh is markedly diminished; one patient has been more or less free for nine months. With the use of the apparatus the improvement of the nasal condition should be progressive. An adult who had used strapping and later an apparatus was able, for the first time in her recollection, to take a full deep breath through the nose.

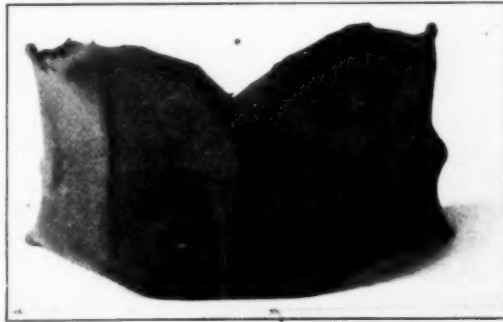


FIG. 3.

Frame with rubber stretched over it.

The length of time that the apparatus must be worn varies. It should be continued until normal respiration is quite established. The patient is then allowed to omit it for a night, then alternate nights followed by its use on one night in three, then one in four and so on. The apparatus should certainly be continued where the conditions of gingivitis and pyorrhœa alveolaris are still unsatisfactory, for every possible effort is necessary for their correction and a return of the mouth-breathing for a short time may be most harmful. The improvement of these conditions is quite remarkable in some patients.

By preventing mouth-breathing in children who have some nasal obstruction but insufficient to demand an operation the nasal respiration may be so improved that surgical interference becomes unnecessary.

This certainly appears to be the case in two or three of my patients. In one of these children, after wearing the apparatus for two nights it was not used on the third night as the mucous membrane had been injured by rubbing. On the night it was omitted the mother said the child's mouth was closed and she was breathing through the nose, but the mouth-breathing occurred on the night following.

This apparatus can also be used to correct conditions which result from mouth-breathing; it is possible to arrange the rubber in such a way that pressure can be brought to bear upon the incisor teeth to correct protrusion. My experience has so far been limited to correction of cases where premolars have been removed, but the possibilities of exercising the function which is normal for the lips in moulding the dental arches seems to be highly probable. There appears to be a valuable use for the apparatus in orthodontics. In one of my cases the frame was made without crossbars, merely the outer wires; studs held the rubber which was put on with very little tension; the teeth were carried back in a most satisfactory manner. At the same time the gingivitis, which was quite marked, was so improved that the mouth appeared almost normal. In another case where the incisors were separated the central vertical bar was divided, allowing the rubber to press on the tips of the teeth; the bar has been shortened gradually. The case is still under treatment. Its early use should prevent some of the changes in the dental arches; protrusion of the incisors might certainly be checked and very probably contraction of the arch prevented.

The uses to which the apparatus can be applied would suggest the name of "artificial lip," for some of the functions of the lips are represented to a considerable degree by it; for instance, the closing of the mouth and the moulding of the dental arches in front. The apparatus may undergo modifications or be replaced, but the principle applied should, I think, be of value.

## Problems relating to the Teeth of the Earlier Forms of Prehistoric Man.

By ARTHUR KEITH, F.R.S.

THE chief problems which at present exercise the minds of anthropologists relate to the nature of the physical characters of Neanderthal man, especially to the characters of the teeth of that ancient and peculiar race. At the end of last century anthropologists had come to regard Neanderthal man as representative of mankind of the Pleistocene period; he was regarded as a stage leading on to the more modern type of man now diffused over the whole earth. At that time—some twenty years ago—the problem of man's evolution was regarded as a comparatively simple one. It was then expected that as we went backwards, in time we should find mankind becoming more and more primitive in structure, more and more simian in its affinities. Indeed, we expected to find, as we went backwards, in time, a linear series of human forms, which would link modern man with an ancient simian form, and that Neanderthal man would prove to be one of the later links in the chain which carries mankind into the far past. This simple conception was disturbed by Professor Schwalbe, of Strassburg, early in the present century;<sup>1</sup> from an examination of the physical characters of Neanderthal man, he came to the conclusion that this race formed a totally distinct species of humanity, that when found there could be no difficulty in recognizing its remains, so differently were they shaped and formed when contrasted with the remains of modern man. No intermediate forms between the two types are known, and Professor Schwalbe concluded that Neanderthal man was not an ancestor of modern man, but represented a collateral species which had become extinct in the Pleistocene period. Professor Keith admitted that he was at first unconvinced by the facts and reasoning advanced by Professor Schwalbe.

Dr. Paul Adloff's famous paper<sup>2</sup> on the teeth of the Neanderthal people, founded chiefly on those discovered by Dr. Gorjanović-Kramberger, at Krapina, Croatia, served to emphasize the truth of Schwalbe's

<sup>1</sup> Schwalbe, "Die Vorgeschichte des Menschen," Braunschweig, 1909.

<sup>2</sup> Adloff, "Das Gebiss des Menschen und der Anthropomorphen," Berlin, 1908.

opinion. From the peculiar characters of the Krapina teeth, Dr. Adloff came to the conclusion that Neanderthal man, at least the Krapina form, could not represent a stage in the evolution of modern man. The features on which this conclusion of Dr. Adloff's is based will be seen from fig. 1. The lower right molars of three dentitions are shown: (1) Modern Europeans; (2) the Heidelberg molars; (3) the molars of one of the Krapina series, that of a lad in which the premolars and last molar are not yet erupted. In the modern mandible the body of the tooth containing the pulp cavity is supra-alveolar, only the roots are embedded in the mandible. It will be observed that in passing from the first to the third molar the pulp cavity tends to enlarge at the expense of the roots, and that the body of the tooth tends to become embedded more and more within the alveolar process of the jaw. In the Heidelberg mandible, which represents by far the most ancient remains of the Neanderthal type yet discovered, the tendency seen in the last molar of modern man is much exaggerated. In all the molars the pulp cavity is large and the body of the tooth tends to be implanted in the alveolar border. As in modern man, the tendency increases from the first to the last molar. In the Krapina teeth the tendency is so marked that the pulp cavity extends deeply into the region of the roots, and the body of the tooth is enlarged at the expense of the roots. The tendency may culminate as in the figure shown of the Krapina teeth (fig. 1) by the inner root septa, or inner walls of the roots, forming a mere cap or lid at the lower or alveolar end of the prismatic body of the tooth (*see* fig. 1, a).

We are thus made aware of a curious process or condition of the molar teeth for which we ought to have a distinctive name, a tendency for the body of the tooth to enlarge at the expense of the roots. It is a tendency to assume the condition seen in the teeth of ungulate or cud-chewing mammals, the condition seen in the ox. For this condition or tendency Professor Keith proposed the name of "taurodontism." The opposite condition—that seen in the teeth of carnivora—where the body of the tooth is above the alveolar border, he proposed the name of "cynodontism." The names he regarded as capable of improvement and brought them forward provisionally. There can be no doubt as to the reality of the processes or conditions the names represent. It was the degree of taurodontism in the Neanderthal teeth, a specialized or retrograde, not a primitive feature, which led Adloff to the belief that Neanderthal teeth did not represent a stage in the evolution of modern teeth, which are more cynodont or primitive.



He was also aware that it was not very rare to find a marked degree of taurodontism in the last molars among modern Europeans.

Two years ago the nature of Neanderthal teeth was brought home to Professor Keith by a discovery made in a buried cave at St. Brelade's Bay, in the south coast of Jersey. Ancient hearths, with flints of the Mousterian period, and remains of Pleistocene animals were discovered and with them a number of human teeth. On being shown these teeth by Mr. R. R. Marett, he had no difficulty in recognizing from their characters that they were those of an individual belonging to the

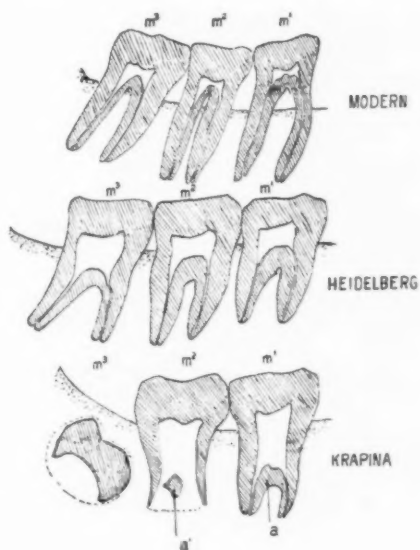


FIG. 1.

Drawings from skiagrams of the lower right molars of (1) modern European, (2) Heidelberg mandible, (3) a Krapina mandible; *a*, *a'*, inner root septum: (1) and (2) after Schoetensack; (3) after Kramberger. (Natural size.)

Neanderthal species of man. There was no need to give a description of these teeth, as Mr. Knowles and Professor Keith had published a full description of them in the *Journal of Anatomy and Physiology*, 1911, xlii, p. 12. The teeth found were members of a single dentition, and the molars showed a high degree of taurodontism. The other teeth, premolars and incisors, also showed a tendency to thickening and enlargement, not elongation of their roots. One illustration (fig. 2)

will suffice to show the characters of the Brelade dentition. The illustration shown in fig. 2 is that of the second left lower molar. The fusion of the roots is not due to an approximation of the roots, the result of a retrograde development, but it is due to an opposite process, the extension of the body of the tooth into the region of the roots, with a fusion of the roots owing to a hypertrophy of their substance. The condition supports Adloff's contention—viz., that it represents a specialization. The teeth of the Gibraltar skull show a similar condition, a marked degree of taurodontism. There is no doubt that the degree of taurodontism varied widely in the examples of Neanderthal man so far discovered. It was extreme in a number of the Krapina specimens; it was less marked in those found at Spy, but in every case the degree exceeded that found in any modern race. Gorjanović-

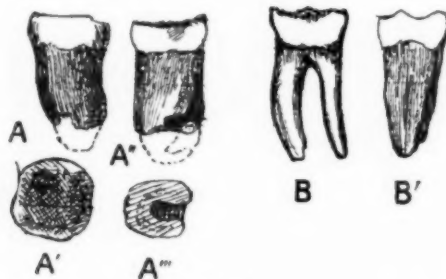


FIG. 2.

A labial aspect of second lower molar of Brelade dentition. A', its chewing surface; A'', distal aspect; A''', section of root; B, labial aspect of the same tooth of a modern English dentition; B', the distal aspect of the same. (Natural size.)

Kramberger had pointed out that the condition occurs in the Eskimo, but a slighter degree is represented than in any form of Neanderthal man. Taurodontism is a character of Neanderthal man's dentition. Lately Professor Keith had visited the Royal Museum at Brussels, where Dr. Rutot gave him an opportunity of examining his extensive collections of Pleistocene fossils and implements. Amongst those was the Naulette mandible: the tooth sockets are shown in the photograph (Dr. Rutot's) reproduced in fig. 3. With the photograph is reproduced a drawing giving the size of the dental crowns; they apparently increased in size from the first to the third, with outlines which show the fusion of the roots. From the condition of the tooth sockets there could be

no doubt that the Naulette mandible—probably that of a woman—manifested a high degree of taurodontism.

When Dr. Adloff's paper appeared in 1907, Professor Keith questioned the validity of the reasoning employed. It was some years later, when recent discoveries of Neanderthal man were made in France, and when it became apparent that Neanderthal man, so far as concerns the later part of the Pleistocene period, was sharply limited to one particular period—the Mousterian—that the conviction was forced upon him that Schwalbe, Adloff, and Dr. Rutot, of Brussels, were right in excluding

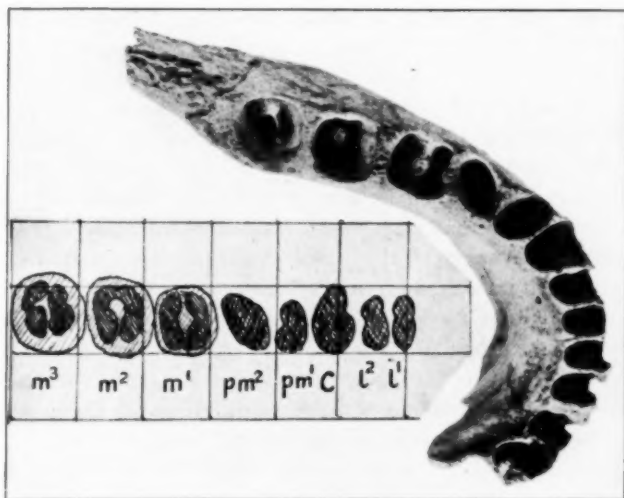


FIG. 3.

The tooth sockets of the Naulette mandible (Rutot). Inset is a sketch of the probable size of the molar crowns and dimensions of the roots.

this primitive race from our ancestry. No geological section yet exposed gave a better idea of the distribution of man in the Pleistocene period than the strata of the sand-pit at Mauer, near Heidelberg, where the famous mandible was discovered by Professor Schoetensack in 1907. The strata are reproduced diagrammatically in fig. 4. The mandible was discovered at a depth of a little over 76 ft., towards the bottom of a series of river-bed deposits known as the Mauer sands. The strata in which the mandible was found belong to an early part of the Pleistocene period. It is probable that the more recent of the Mauer sands belong

to that period of Pleistocene culture known as the Chellean. Then follows the deposit of ancient loess representing the Acheulean period. The Mousterian period—the one to which the various remains of Neanderthal man have been ascribed—is represented at the junction of the ancient and recent loess. Then follow the deposits of recent loess—the formation of which appears to cover the later phases of Pleistocene culture—the Aurignacian, Salutrean and Magdalenian. We know a considerable number of remains of men who have lived in these latter periods—the Magdalenian, Salutrean and Aurignacian. They are people like ourselves, their teeth and ours belong to the same type. When we pass into the older Mousterian period the type of man changes. No representative of modern man of that period has yet been discovered in Europe; all the men so far found in strata of the Mousterian culture are Neanderthal in type. It is impossible to believe that in the passage from the Mousterian to the Aurignacian periods the inhabitants of Europe were suddenly altered in type: the only possible explanation is that Europe was invaded by a type—the modern type—of man who replaced the Neanderthal man. The historical sequence in the Pleistocene period is in favour of the contention that Neanderthal man was not transformed into modern man, but became extinct when Europe was invaded by the modern type of man, who seems to have been evolved outside Europe.

The statements so far given merely serve as an introduction to another problem, the problem of the Galley Hill man. Four years ago, when Professor Keith was preparing a small book on "Ancient Types of Man," he was still dominated by the idea that Neanderthal man was the only form of Pleistocene man and represented a stage in our evolution. He realized then that Galley Hill man was out of place, if the stages of man moved steadily forwards in progressive stages to the modern type. At that time there was still doubt as to the relationship of our river valley deposits to the various cultural cave strata of the Continent. Accordingly, he was prepared to think that a fuller knowledge of Pleistocene formations would show that in point of time Galley Hill man would come after Neanderthal man. The opposite has proved true; the Acheulean and the Chellean cultures belong to an infinitely older part of the Pleistocene period than the Mousterian, the culture of the Neanderthal period. The 100-ft. terrace in which the remains of Galley Hill man was found was laid down during the age when the Chellean culture prevailed in the Thames Valley—the Mousterian culture belongs to more recent deposits laid down when the valley had

nearly reached its present form and depth. One easy solution of the difficulty is to regard the Galley Hill as an interment of a more recent date than the deposition of the 100-ft. terrace. Those, however, who have examined the evidence relating to the discovery of the Galley Hill skeleton can find no loophole of escape; all the evidence points clearly

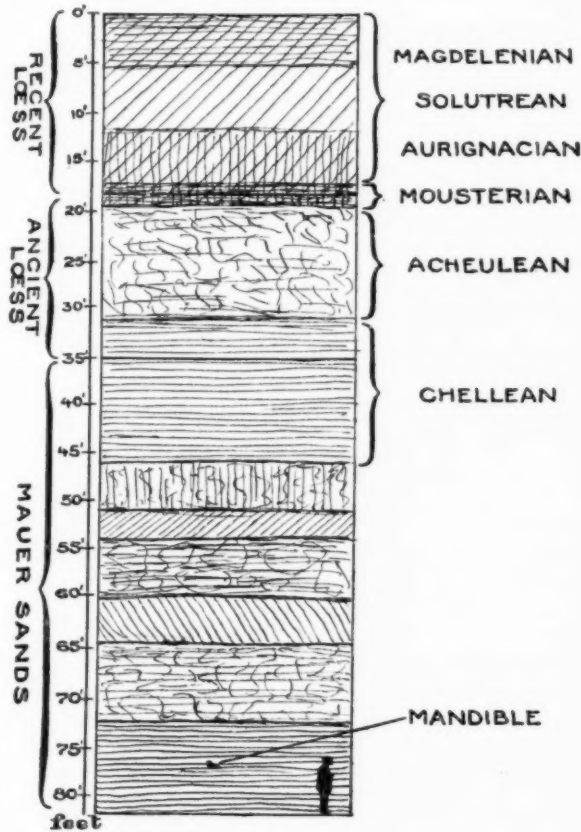


FIG. 4.

Section of the strata at the sand-pit of Mauer, showing approximately the periods of culture in existence when the various layers were deposited.

to its age being contemporaneous with the formation of the 100-ft. terrace. The real evidence against its authenticity is, that it is in type of skull, teeth, and limb-bone of the modern human form, and cannot, therefore, be older than the more simian form—Neanderthal man.

When, however, we look at the teeth of Galley Hill man we must admit that they are really more primitive or simian than even the teeth of Neanderthal man. In fig. 5 four molars are represented, amongst them, B, the second left lower molar of the Galley Hill mandible. The roots are short and not widely separated; the crown and body are above the alveolar border. On one side of the drawing (B) is placed the chimpanzee's second lower molar (C); on the other side the corresponding tooth from a modern English jaw. The second left molar from the Brelade dentition is also shown (D). It will be seen that the least simian—taking the chimpanzee's molar as our type—is the Brelade or Neanderthal tooth; the Brelade tooth is the most specialized or taurodont. The tooth of Galley Hill man in this respect is more positive or simian than that of Neanderthal man; there is nothing in its form which precludes us from attributing to it the antiquity suggested

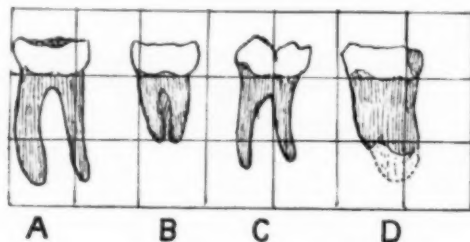


FIG. 5.

The second left lower molar of modern English jaw (A); Galley Hill (B); Chimpanzee (C); Neanderthal (D). (Natural size.)

by the site in which the Galley Hill skeleton was discovered. The teeth of many examples of Pleistocene man of the modern type have short roots.

As no minute description has been given of the Galley Hill teeth, the drawing represented to scale in fig. 6 may be welcome. Only one half of the mandible was found, with the premolar and molar teeth in situ. As in modern teeth there is a slight increase in taurodontism as one proceeds from the first to the last molar. There are five cusps on the crown of each of the lower molars. The length or medio-distal diameter of the crown of all three is approximately equal, 11 mm., the middle tooth being slightly the smaller, the labio-lingual diameter of the crown is slightly less than the medio-distal diameter, 10.5 mm.; whereas in Neanderthal man the width is usually greater than the

length of the molar crowns. In the proportion of the diameters of the molar crown the Galley Hill teeth are the more simian, the medio-distal diameter of  $pm^1$  is 6.5 mm.; of  $pm^2$  6.8 mm. Thus, although like modern teeth, the Galley Hill dentition is in reality more primitive or simian, and less specialized than the teeth of Neanderthal man; far from refusing the Galley Hill remains as authentic because of their characters, we ought to accept them if the evidence of their geological age is sound.

What principles are we to apply in determining the degree of primitiveness to any given dentition? The condition of taurodontism has been already mentioned. It does not occur amongst primates, at least amongst those who have a structural relationship to man. We

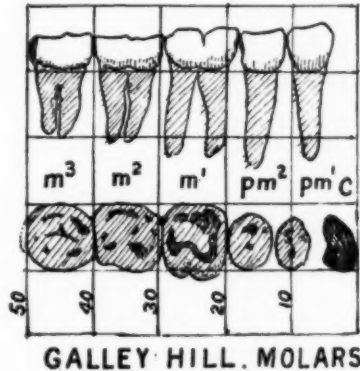


FIG. 6.

Drawings of the premolar and molar teeth of the Galley Hill skeleton.

must regard its presence in Neanderthal man as a specialization which takes that race away from the ancestral line of more modern man. It is probably a modification correlated with the nature of diet, a root or vegetable diet, requiring greater grinding power. The shape of the palate of Neanderthal man—but as yet we know very little of the shape of his palate—indicates a peculiar specialization. In fig. 7 is represented a drawing made to scale of the palate of the Gibraltar cranium, the earliest discovered of all the remains of Neanderthal man. Beside it is placed the palatal arcade of a native Tasmanian. Of the two the Tasmanian palate is the more simian; the molar sides of the arcade assume the parallel arrangement seen in anthropoid palates.



The Gibraltar palate is horseshoe in form; it has become specialized as regards width rather than as regards length. The sagittal length of the Tasmanian dental arcade is 65 mm.; the Gibraltar palate is 54 mm. in length (see fig. 7); in width the latter is 70 mm.; the Tasmanian 68 mm. In shape of palate Neanderthal man is not so primitive as the native Tasmanian, or Galley Hill, or of modern Europeans.

There is another condition which we seek for when estimating the primitive nature of any given dentition. The condition is illustrated in fig. 8. We suppose that in a primitive dentition the size of the molar crowns should increase from first to third. We are really dealing with a physiological condition which is well illustrated by comparing the molar dentitions of the gorilla and chimpanzee (see fig. 8). Of the

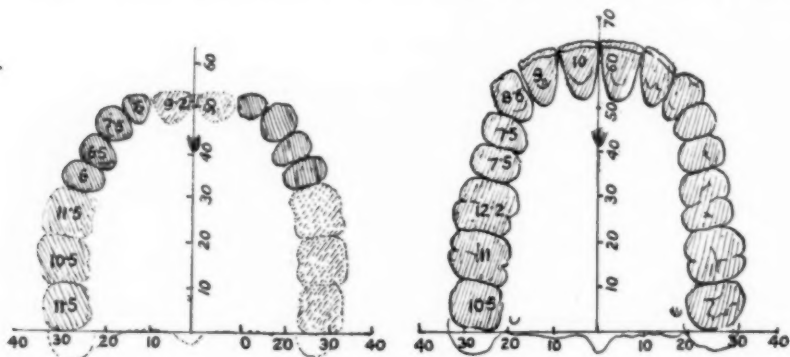


FIG. 7.

The palatal arcade of the Gibraltar cranium compared with that of a Tasmanian, in the Museum of the Royal College of Surgeons. The scale is indicated in centimetres, and the medio-distal diameters are marked on the crowns of the teeth.

close structural and genetic relationship between these two anthropoids there can be no doubt; it is in some cases impossible to tell whether a given brain is that of a gorilla or of a chimpanzee; so like are they. There is also no doubt of the close structural relationship between these anthropoids and man. Hence any observation on dentitions of those two anthropoids has a direct bearing on the problems relating to the evolution of man's dentition. The dentitions of the gorilla and chimpanzee are very different; they represent opposite stages of a process of tooth development for which we have no good term. In the gorilla the crowns of the lower molars increase from the first to the third, in the

chimpanzee the last is usually the smallest of the series. In the upper molars, the third is distinctly the smallest of the series in the chimpanzee, but in the gorilla it is but a little less than the first. The crowns, cusps and roots of the gorilla's molars have a more robust development than in the chimpanzee. The molar length of the gorilla represented in fig. 8 is 52 mm.; in the chimpanzee 35 mm. We have every reason to suppose that the gorilla and chimpanzee dentitions are derived from a common form—the gorilla's representing a progressive, and the chimpanzee's a retrogressive development from that common form. The term wanted is one to indicate these opposite phases of a common process. If the orang dentition (see fig. 9) be taken as representing a mean or plenal degree of development, then the gorilla's dentition

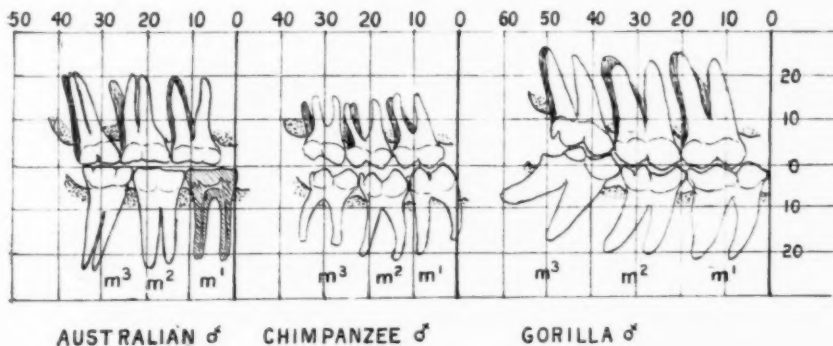


FIG. 8.

The molar dentition of a native Australian compared with those of a chimpanzee and a gorilla. The scale is represented in millimetres.

represents a supra-plenal phase, and the chimpanzee's the infra-plenal phase. When dealing with human teeth we have always supposed that an infra- or sub-plenal phase—one in which the third molars were, on the average, smaller than the second molars—represented a degenerate, and therefore a modern form. We find, however, that various forms of primates—both ancient and modern—may show a sub-plenal phase. The chimpanzee is as "primitive" as any human ancestor we are ever likely to find, yet we find its teeth in this sub-plenal phase. It is clear then that we cannot apply the law of plenal molar development as a sure criterion of either modernity or of antiquity of any given form. So far as the lower molars of the Galley Hill man is concerned the plenal form is represented. As a rule the Neanderthal

lower molars show the supra-plenal condition. From fig. 8 it will be seen, that although the crowns of the chimpanzee's dentition represent a retrogressive phase, the roots do not undergo a corresponding alteration. In even the most primitive of modern dentitions (*see* fig. 8), the roots of the distal molars do show a tendency to fusion. We must suppose that man comes of a stock in which the roots were widely and separately implanted in the alveolus, and we expect that the very early forms of man will show discrete and widely separated roots.

In fig. 9 is shown the degree of plenal development of molars in anthropoids and man. It will be most convenient to consider first the development in modern Englishmen. The diagram in fig. 9 represents the mean molar development in twenty-two English medical students—measured from impressions taken on plates made of paraffin wax. The upper molars decrease from the first to the third—the medio-distal diameter of the crowns being 10·3, 9·4, and 8·6 mm. The mean development of cusps is also given in the table—3·9, 3·6 mm., and 2·8 mm., showing the degree of retrogression in cusp development. In the lower molars there is also a decrease from first to last, the measurements being 10·2, 10·1, and 9·1 mm., and there is a corresponding retrogression of cusp development represented by 4·2, 4·7, and 3·7 mm. cusps. The condition of the molar development is markedly sub-plenal. This is also the case, but to a less degree, in the Tasmanian molar development (*see* fig. 9). In Neanderthal man the dentition, so far as relates to the size of the crowns, is supra-plenal—the table being compiled from all available measurements—the lower molars increase from the first to the third; in the upper molars the second and third are of nearly equal size. As regards cusp development the Neanderthal teeth show a degree of retrogression almost as great as in modern Europeans. The upper and lower third molars are irregular and anomalous as regards their cusp development. It is unnecessary to analyse in all their details the formulæ given in Table 9 for the molar development of the gorilla, orang and chimpanzee. As already said, in size of crown and in cusp development, the gorilla represents the supra-plenal, the orang the plenal, and the chimpanzee the sub-plenal degree of molar development.

The table is founded on measurements made of anthropoid dentitions in the various London collections, numbering in all about 150 individuals. It is also easy to see that retrogression and progression affects the molar teeth in a definite order. The third upper molar is the first to be affected, either in progression or retrogression; the postero-internal

cusps is the first to become reduced, to become irregular, or in the progressive form to become stronger. When the change, be it progressive or retrogressive, proceeds further, the second molar becomes affected, the postero-internal cusp being the first to manifest the change. The first molar is the most conservative, and the least liable to alter either in progressive or retrogressive changes. In the lower series the third molar is also the first to alter, its posterior cusps being the point which reflects the phase. Owing to the forward displacement of the lower as

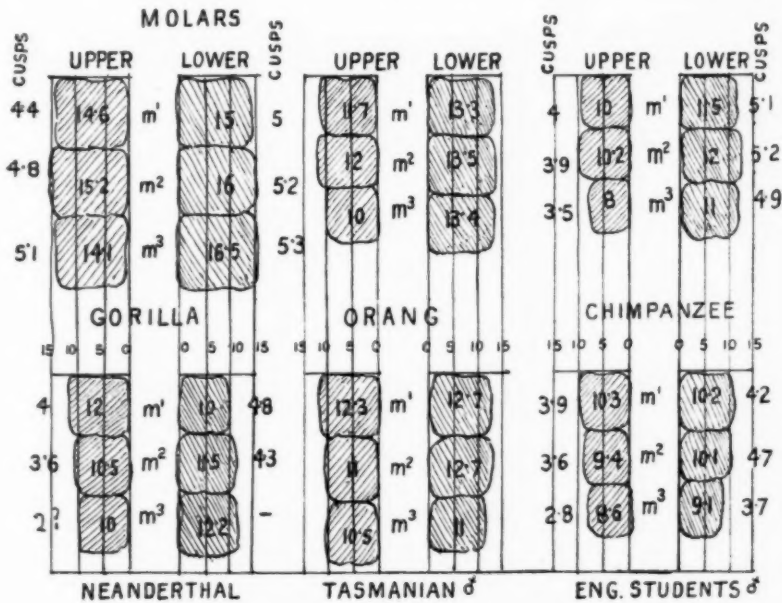


FIG. 9.

Diagram showing the development of molars in various forms of the higher Primates; the teeth are placed in the diagram so as to contrast their length or medio-distal diameters. The parallel lines which cross the length of the crowns are 5 mm. apart. The cusp development is also given in the diagram.

compared with the upper molars, the change in the third lower molar is later in appearing than in the corresponding upper molar. As in the upper series, the first is the most stable tooth—the least liable to be affected in either progressive or retrogressive changes. In supra-plenal dentitions it is the smallest of the lower series; in sub-plenal forms it becomes the largest. It will be thus seen that even in primate

dentitions, which are of an ancient or primitive type, as are those of the great anthropoids, various degrees of plenal molar development are found.

We are therefore justified in inferring that, in the various species or genera, into which the earlier forms of man must have branched, similar degrees of plenal development had occurred. If, therefore, we find forms of man with a sub-plenal development, that feature need not indicate that the form is of recent date. On the other hand, we must recognize that there is a marked tendency amongst all highly civilized modern races to a subplenal molar development, and unless the geological evidence is to the contrary, must presume that a marked degree of molar retrogression is a presumption in favour of any given dentition being of a modern date. Contracted palates, and crowded, irregularly placed teeth, have not been seen in human remains which belong to a period preceding the Bronze Age.

In fig. 10 is reproduced Dubois's drawing of the third upper molar of *Pithecanthropus*. The roots are short, stout, and widely spread. The two labial roots are fused, but there is no trace of the taurodont condition seen in all Neanderthal teeth. We have certainly in this tooth the representation of a primitive human form. The actual dimensions of the crown are great: the length or proximo-distal diameter of the crown is 11·3 mm., its width or labio-lingual diameter 15·3 mm. The fusion of the labial roots, the reduction of the two posterior cusps to form a crenulated distal margin for the crown, show that in this extremely primitive human form the dentition was reduced or sub-plenal. Unfortunately no figures of the two premolar teeth have been published. They should throw further light on the peculiar nature of *Pithecanthropus*.

The discovery of the Piltdown skull by Mr. Charles Dawson adds to a rapidly growing list a very primitive form of ancient man. The molar teeth show no degree of taurodontism; they show the opposite condition cynodontism. The three molars were probably of about equal size; there is a degree of fusion of the roots of the last molar. There are five cusps on each molar present. The molar development is plenal. Further details of the dentition will be found in Dr. Smith Woodward's paper, and in Professor Underwood's account of the teeth. The main interest of the Piltdown dentition relates to the region of the canine teeth. The evidence is decidedly in favour of a simian development of the canine teeth in that individual—as the authorities who have investigated the remains have declared. That a human form should be discovered with a large canine tooth was expected by all of those who recognized the

close structural relationship between man and the great anthropoids and the manner in which the canine tooth is developed and formed in modern man.

In fig. 11 is represented various degrees of the canine development met with in the higher primates. The teeth are drawn to scale with the palate placed in true profile. Four individuals are represented in fig. 11, a native Australian with a well-developed dentition, a female chimpanzee, a male chimpanzee, and a gorilla. These individuals represent various degrees in the plenal development of the canine region of the palate. The changes in this region—both progressive and retrogressive—proceed independently of the changes affecting the molar region. The molar series of the Piltdown mandible has a total length of about 36 mm.; the three molars were thus of moderate size, but the teeth of the canine region must have reached dimensions far

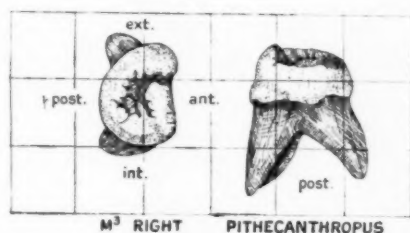


FIG. 10.

Two views of the third upper right molar of *Pithecanthropus* (after Dubois).  
The squares represent centimetres.

beyond any human dentition yet known. Amongst higher living primates the teeth of the canine region of the jaw find their maximum development in the male gorilla. In the specimen shown in fig. 11 the teeth of the anterior or canine region extend in an antero-posterior or sagittal direction—from the crowns of the mesial incisors in front to a line joining the distal margins of the second premolars for a distance of 52 mm. (see fig. 11); in the male chimpanzee the extent is 45 mm.; in the female chimpanzee 57 mm.; in the Australian palate shown in fig. 11, 27 mm. Using the same terms as before, it may be said that in the male gorilla caninism reaches a supra-plenal degree; in the Australian, an infra-plenal development; while in the female chimpanzee a mean or plenal phase is represented. The effect of caninism is not confined to the canine teeth alone; the first premolar is affected in every phase of

development of the canine teeth. The first lower premolar is the fulcrum or blade against which the upper canine tooth works; its development and specialization depend on the size of the canine teeth. In turn the first lower premolar acts against the first upper premolar, hence the premolar teeth form an intrinsic part of the canine mechanism.

We are still in ignorance of the exact use of the canine teeth in anthropoids. They are certainly organs of defence or attack, but they are evidently used also for certain masticatory purposes. They are regulated in their degree of development by the same factors as regulate sexual characters by secretions arising in the genital glands. In all modern human races—in all races so far discovered, except that

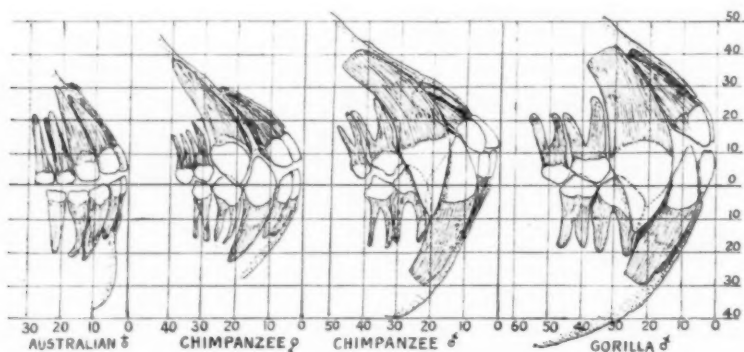


FIG. 11.

Various phases in the evolution of the teeth of higher Primates in the canine region.

to which the Piltdown individual belongs—an extreme retrogression of the canine series has been reached—a marked degree of infra-plenary caninism. Projecting canines have certain disadvantages: they prevent any free side-to-side movement of the jaws in chewing; the long canines imply a scissors-like action in biting and chewing. With the disappearance of the canines a side-to-side movement of the molar crowns becomes possible, and it is strange that the chewing surfaces of the Piltdown molars are worn as if there had been a side-to-side movement, and as if the canines had not been long enough to prevent this movement.

Professor Keith was not prepared to find a comparatively large brain—the Piltdown brain falls within the lower limit of human brains as



regards size—accompanied by a degree of caninism so great as is suggested by the Piltdown mandible. It has usually been inferred from the characters of the temporal ridges in the calvaria of *Pithecanthropus*, and from the characters of the last molar, that there was not any marked degree of caninism in that human form. In the Heidelberg jaw the canines have subsided to their modern dimensions, and yet the strata in which the mandible was found belongs to an early phase of the Pleistocene period. The date of the Piltdown man is an open question. Flints of the Chellean period were found with or near the remains; so were those of Pliocene mammals. Seeing that we know that in one species of man at least—the early Neanderthal type of Heidelberg—the canine teeth had receded to a human stage of development at the beginning of the Pleistocene period, it is clear that the Piltdown man should belong to a much earlier date than the Chellean period; it is most probable that it will ultimately prove to belong to a Pliocene in date. We may safely regard the features of the Piltdown teeth and mandible as representative of one genus of man of the Pliocene period.

#### SUMMARY.

In this paper an attempt is made to sketch the various features of a dentition which should guide us in estimating the degree of antiquity, and the degree of primitiveness in any discovery of ancient or fossil man; the teeth of Neanderthal man, although primitive or simian in some features, in others are highly specialized. They show the condition of taurodontism beyond any other known form of man or ape, surviving or extinct. The condition of molars and of canines described here as plenal, supra-plenal and infra-plenal have also to be taken into account. The various plenal phases apparently represent the result of physiological processes, and are usually, but not necessarily, indications of antiquity and primitiveness. As regards the teeth of the Galley Hill mandible, they are essentially more simian or primitive than those of Neanderthal man.

## DISCUSSION.

The PRESIDENT (Mr. P. Sidney Spokes) said it was a great gratification to the Section that Professor Keith had consented to come and give his very important communication. It was common for us nowadays to take more interest than formerly in our ancestors in the remote past; and it was well that those whose work was concerned with the teeth should make themselves acquainted with something which was well authenticated. If it was necessary to part with Neanderthal man, they would give him up with regret. Many members had enjoyed reading the book Professor Keith referred to, and some had attended his lectures at the College of Surgeons with great pleasure. He would have liked Professor Keith to have brought the interesting genealogical tree shown at the College which put out of court that old saying that "man is descended from monkeys," for which at present no scientific man had made himself responsible. Possibly Professor Keith would speak of that to them on a future occasion. He had carried them to the Mousterian period before arriving at man, and he passed over the Chellean and Acheulean periods, where the question of the flint implements and strata came up. The Section had at least one member who was a distinct authority on flints as well as on other things. The way in which Professor Keith laid his observations before the meeting left nothing to be desired, and if the members of the Section did not succeed in finding him those beautiful names of which he was in search, he must be asked to accept their apologies; they would go away and think the matter over, submitting any ideas which might come into their minds.

Mr. G. JACKSON (Plymouth) exhibited some teeth (fossilized) which were found at Plymouth, in limestone caves 20 ft. below high-water mark, during excavations for wharves. He did not think human bones had been found before these teeth were discovered, and teeth found included those which might have belonged to the lion or tiger or rhinoceros. Bones of the cave bear, sabre-toothed tiger, rhinoceros, &c., and of small animals such as the hare, had also been found. Some of the teeth were from the upper jaw and some the lower; some were worn and others not. In the same caves some charcoal was found, and a large flint core. There were no flint flakes or scrapers or arrowheads. Humeri and other bones were found, but not a complete skull.

Mr. UNDERWOOD said he considered that the evolution of the brain was a much slower process than was the evolution of the face; environment might cause a difference in the conformation of the face in a comparatively short geological time. That fact might explain some of the confusion experienced from finds of skulls. That seemed to be a good deal the case with the Piltdown skull, which had possessed a somewhat large brain; yet it had a very early type of jaw. But the opinion was gaining strength that Neanderthal man was not an ancestor, but an extinct thing altogether. He was pleased to hear that

Professor Keith was in agreement as to the raised and large canine in the Piltdown skull, because he felt some responsibility himself in that matter, having strongly maintained that view. He did not think it could be avoided, because the lower border of the jaw was so like the lower border in the chimpanzee. In order to satisfy a few critics the skull was restored, taking a cast of the front teeth, from the canines forward, from a Neanderthal mandible. An attempt was made to make it fit, but it would not, and left a ludicrous space. Still, his idea that the brain changed much more slowly than the face might give some explanation. Also, in the Piltdown skull, the arrangement of the meningeal arteries was simian, as well as the arrangement of the mylohyoid groove, which was simian, although the mandible was, as Professor Keith said, slight. The mylohyoid groove was behind the inferior dental foramen, which was not found in any other human mandible.

Mr. DOUGLAS GABELL said the type of tooth in which there was, as the Professor said, a large pulp cavity extending below the alveolus, was not so very rare in the present day. In a search for odontomes he had found a numerous collection of teeth in modern skulls, always in the upper jaw; he did not know how many might have been found in the same skull. But it was not very rare to find teeth with the pulp cavity going far up into the jaw to an even greater extent than the "taurodont" teeth shown in the Krapina skull.

Mr. PITTS said that, looking at the teeth of Neanderthal man from a dental standpoint and without any special knowledge of anthropology, the large size of the pulp-chamber and the extraordinary nature of the roots suggested the possibility of some special function of the pulp and periodontal membrane different from that in modern man. Perhaps the large pulp-chamber was associated with an unusual power of forming secondary dentine as a provision against excessive attrition. With regard to the roots, it would be interesting to know if a microscopical section has ever been made. In modern man the roots were composed chiefly of dentine with a thin layer of cementum. He thought it possible that in Neanderthal man the amount of cementum might be very greatly increased. Perhaps there was a secondary cementum formation going on throughout life as a normal physiological process.

Mr. A. E. RELPH said one could practically trace the same type of tooth from modern man back to the Mousterian period as represented by the La Chapelle and Le Moustier skeletons. The Galley Hill skeleton, which was earlier—Acheulean or even Strépy—showed no marked differences, while the finds at Ipswich and Piltdown carried the modern type well towards the Pithecanthropus of Java and so to our simian ancestor. It was only in the Krapina and Jersey teeth that the remarkable condition of the pulp area and roots was found, but the remains of the so-called Neanderthal race were not earlier than the Mousterian period, and in the earlier type of this race as represented by the Heidelberg mandible these conditions were not nearly so marked. Did this formation of the pulp chamber and roots occur in a special race progressing from the Heidelberg mandible to the extinction of that race

in Mousterian times? Or, was this condition and the peculiar formation of the skull that went with it due to abnormal activity of the pituitary gland occurring in what would otherwise have been an individual of the ordinary type of the period?

Professor WILLIAM WRIGHT said there was a great gulf between his position and that of Professor Keith on almost all the questions he had put before the Section. He (the speaker) did not think Neanderthal man was specifically different from man of the present day, though he admitted no present-day man had *all* the characteristics of Neanderthal man. Reading through Schwalbe's papers, he came to the conclusion that that authority was very unfair in the evidence he adduced. Schwalbe paid but little attention to Spy 2, because that specimen did not sufficiently support his theory, and when he said Neanderthal man did not exist at the present time, he did not pick out a typical Australian skull, but one which was in type more European than most Australian skulls were; and he contrasted this European-Australian type with the most advanced type of the Neanderthal race which he had at the time. There seemed to be no different standard of culture associated with Neanderthal man. Taking the flints, beginning with the Chellean period, there was found to be a slow and gradual development. There had been no break such as we might have expected had Neanderthal man been something less than man. Whether Neanderthal man was man or not, he acted and reasoned as man; the mind and the fingers were those of man. With regard to the odontological points, he did not know whether Professor Keith had considered sufficiently, when he spoke of the position of the crowns of the teeth and the alveolus, the shrinkage of the alveolus. It was not difficult to find samples at the present time where the crown of the tooth was high above the alveolus, and other places where it was almost on it. That was due not so much to changes in the tooth as to changes in the alveolus; and there was no doubt that prehistoric man suffered much from alveolar disease; in support of that one had only to look at the jaws of the men living in the Bronze or the Iron Ages. He did not know that there was any portion of human anatomy more subject to variation than the teeth, and a classification of man upon his teeth was about the most shifting sand one could build upon. A friend near him had pointed out the great variability in the size of the pulp cavity, and in a paper which he (the speaker) read to the Odontological Society some years ago he laid stress on the Krapina teeth as something entirely different from teeth of the present day. But on going deeper into the matter, and with a wider acquaintance with dental variations, that impression had faded away. In any well-equipped museum it was easy to find teeth like Krapina teeth, so far as the roots were concerned, and he considered Mr. Pitts was correct in thinking it was due to some growth of the cementum, which had brought about a fusion of the roots. The difficulty of knowing what men of those far-off days were really like was very great. It had been said that truth dwells at the bottom of a well, but surely the deepest of all wells was that of archaeology.

Mr. HARRY BALDWIN said he thought the temporary teeth in man had not been sufficiently studied in relation to teeth of ancestral types. There was a great difference between the anatomical characteristics of temporary teeth in man and the permanent teeth. The infantile characteristics in an animal showed kinship to its far-off ancestral relations, more than did the specialized adult forms. The temporary teeth in man had many characteristics in common with the simian type of teeth, which permanent teeth had not. The broad flanges in the Neanderthal type, referred to by Professor Keith, suggested the flanges often seen connecting the roots of the temporary molar teeth of man. The broadly splayed roots of the temporary teeth in man were broadly splayed to contain the developing premolars, but after making allowance for this, it would be a useful form of study to compare the present-day temporary teeth with the permanent teeth of those ancient types. Again, similarly, the lower jaw of a present-day infant of about a year old was in general outline comparable with some of those very ancient lower jaws. So it would be a useful form of study to compare the temporary set in man with those ancient forms.

Professor KEITH, in reply, said the teeth brought by Mr. Jackson were fossilized, and they were not Neanderthal, and, from their accompaniments, undoubtedly of a Pleistocene age. He did not know why remains of Neanderthal man had not been found in England, but he thought it likely that such would be found. Some very suggestive points had been brought forward in the discussion. He agreed with Mr. Baldwin that much remained to be done in the investigation of temporary teeth. It was very likely that the temporary teeth would retain primitive features to a greater extent than the permanent teeth. Members of the Section had done much towards getting a good consensus as to the amount of disease, but there was still needed a morphological census of English teeth. He had been glad to hear his old opponent, Professor Wright, and it was refreshing to find they still failed to agree. He (Professor Keith) had put himself to considerable trouble to learn the variations in modern dentitions, and if anyone would show him one which resembled the Neanderthal form it would be the first time he would have seen it. A short time ago his friend, Professor McKenney Hughes, of Cambridge, contributed an article to *Nature*, giving an account of the discovery of a Neanderthal skull at the bottom of a bog, adding that it was probably the skull of a monk belonging to an early Christian period. The first glance at the drawings given with the article showed Professor Keith that the skull was as opposite to the Neanderthal type as any skull could be. It was a Bronze Age skull in all its features. He held it to be very important that he should combat all the prejudices against the antiquity of the modern type of man, and he was glad to find Professor Wright still standing up for the old beliefs. It was very important for the future that they should have a free field, free from certain preconceptions. He wanted to destroy the prejudice which prevented discoveries of teeth and skulls of the modern type being at once adjudged as recent burials; he was anxious that nothing should be rejected because of its modern form. He was no authority on flints,

and he was glad there was someone present who knew them. His friends told him the Mousterian flints were retrograde when compared with older forms. He had examined the top of a skull which was found at Bury St. Edmunds in brick earth 7 ft. down, along with Acheulean flints. It certainly did not belong to the Neanderthal type, yet belonged to a period older than the Mousterian. The Galley Hill skull was Chellean in date. If that was not so, geological evidence was valueless. Neanderthal man came with the Mousterian civilization, but when that civilization went he went. He was putting forward what was accepted by many men. The key to the present situation was the belief in a linear series of ancestors. If one wanted to know what primitive humanity must be like, one must go to the most primitive relatives of man available—the orang, the chimpanzee, and the gorilla. It must not be supposed that one was the ancestor of the other; they were all cousins. Similarly there were probably many genera of primitive man. Neanderthal man represented a late representative of an extinct genus. Modern man appeared to be the sole surviving form of the genus of man that ultimately proved to be the most successful. The date of his evolution had still to be fixed. He agreed with Mr. Relph that the peculiar form of the roots of Neanderthal teeth was probably due to a peculiarity in the nature of the periodontal membrane, and in the amount of cementum formed round the roots.

## Odontological Section.

May 26, 1913.

Mr. P. SIDNEY SPOKES, President of the Section, in the Chair.

### Discussion on Mr. W. W. James's paper on "The Cure of Mouth-breathing."<sup>1</sup>

MR. DOUGLAS GABELL said he had previously had an opportunity of seeing this apparatus, and had put a good many of them into use. What surprised him, first of all, was the comfort with which the patients wore the apparatus. Among twelve or fifteen cases he had not received the least complaint, and no discomfort was experienced during sleep. Mr. James had cut his description rather short, because he said but little about the use of the apparatus for regulating the teeth or undoing the damage previously done to the teeth by mouth-breathing. It was a happy idea, because the troubles due to mouth-breathing were remedied naturally. One could restore the pressure on the front of the teeth, which the raised upper lip lost, by so placing the little vertical bars that the apparatus rested slightly on the front teeth, and at the same time remove the pressure of the cheeks on the premolar region by widening the frame at the side. It must be done gently, otherwise there was considerable pressure and pain. In one patient who had worn the device a month there was a noticeable drawing-in of the four upper incisors by wearing the plate at night-time only. The more one pressed outwards in the premolar region the more pressure there would be inwards on the upper front teeth: it was held in by the pressure of the cheeks. By cutting vertical wires, and bending them slightly, one could regulate the pressure on any tooth to exactness. He had one patient, a very intelligent girl, aged 18, who had worn this apparatus two months. Recently she had a cold in the head, and had to leave the apparatus off, because it was so efficient that one could not breathe through the mouth when it was in position. She complained that she could not sleep comfortably when breathing through the mouth as she had formerly done. That showed she was losing the habit of mouth-breathing. It was as yet early

<sup>1</sup> Adjourned from April 28.



to speak about ultimate results, but the result of it on gingivitis in the front of the mouth was very marked. A patient whom he saw at the hospital had been wearing it for two months in consequence of marked superior protrusion and hyperplastic front teeth, with very bad gingivitis in upper and lower jaw. She returned to the hospital last Wednesday, and he found that the gingivitis in the upper jaw had entirely disappeared, and very little remained in the lower jaw. All these patients, after wearing the apparatus one or two nights, remarked how comfortable their mouths were in the morning, and how much easier it was to keep the front teeth clean. He considered it a very valuable additional means of dealing with irregularities and breathing through the mouth. Hitherto it had been easy to clear the nose so as to make it possible to breathe through it, but it had been difficult to break the mouth-breathing habit. One patient told him that she found that directly she put the apparatus into position it soothed her to sleep, much as the "dummy" was supposed to do.

Mr. LEWIN PAYNE thought the Section was much indebted to Mr. James for bringing his apparatus forward; it was a matter of interest to them all to do their best to stop mouth-breathing. Four months ago Mr. James kindly showed him the apparatus, and he thought the idea so admirable that he put it into use at once. His experience had been much the same as Mr. Gabell's: not only did it stop mouth-breathing when properly fitted, but it was easily adapted and worn with comfort. With regard to Mr. Colyer's mention of the vulcanite mouth screen reported in the *Dental Cosmos*, only three or four weeks before that article appeared, when experimenting with the apparatus, he (the speaker) made a similar one to that recorded in the *Cosmos*, with the exception that he did not use soft rubber round the margin. After the appearance of the article in the *Cosmos* he tried one with a soft rubber margin, but he found it less comfortable. As he was himself a mouth-breather and had used the device, he could speak from experience. A vulcanite appliance forming a screen with a thick margin was, in his opinion, the most comfortable, and it had some advantage over the metal wire screen, in that it required no addition of rubber dam, and it proved as easy to clean as the metal screen. With regard to the possibility of retracting incisor teeth, he had tried it in two instances, and it certainly had done the work which Mr. James claimed for it, though he could not submit any measurements. He considered that this was a matter upon which Mr. James deserved congratulation, because it set forth a principle which permitted of many useful modifications in the future.

The PRESIDENT (Mr. P. Sidney Spokes) said he remembered reading, some years ago, of an apparatus, not like Mr. James's, to keep the mouth closed while the patient slept. Perhaps Mr. James could claim priority for his apparatus over that alluded to by Mr. Colyer, as he had been using it for some time before he brought it forward. One never quite knew where one was in the matter of priority; for instance, he saw the day before a very interesting

pamphlet published in 1849, in which the author, who was then aged 21, had already worked out the germ theory of disease, and pre-dated the theory of evolution. The President of the Linnean Society had taken that pamphlet as the text for his address, which would soon be published.

Mr. JAMES replied that he had not read the article referred to, but that he had tried a vulcanite apparatus. An apparatus made of vul rubber entirely was comfortable, but it was difficult to get a good surface. He found his own apparatus as shown was the best of those he had tried. He did not know that it was not better with thinner wire than in the one illustrated. He thanked Mr. Douglas Gabell and Mr. Lewin Payne for their appreciative remarks.

### **Specimen of Supernumerary Tooth.**

Shown by J. G. TURNER, F.R.C.S.

MR. RUPERT CLARKE, of Reading, had asked Mr. Turner to present the specimen to the Museum. It was taken from a girl, aged 18. At the age of 7 Mr. Clarke took out the temporary tooth. At the age of 16 he took out the succeeding permanent tooth, because it had been broken two years before and was abscessed. After that the supernumerary tooth erupted in place of the upper central. It was obviously a supernumerary tooth, of very pretty form, like a lotus flower. On the front of one of the cusps was a facet. The girl had inferior protrusion.

### **An Odontome of the Premaxilla.**

By LEONARD HARWOOD, M.R.C.S., L.D.S.

THE rather unusual occurrence of an odontome in the premaxilla must be my excuse for showing this specimen. The patient was a female, aged 22. Her dental history is that all her temporary teeth erupted properly with the exception of her left maxillary incisors. These teeth formed a lump in the jaw and were removed at the National Dental Hospital in 1908. As far as I can ascertain there was nothing abnormal about them. As regards her permanent dentition, there has been normal eruption of all the teeth except the left maxillary incisors and canine.

JU—15a

The patient first came under my notice in April of this year and was apparently edentulous, the other teeth having been extracted for caries. There was a marked swelling in the region of the left premaxilla, and a small portion of enamel was visible through the gum. The X-ray which I now show was taken, and this clearly demonstrates the presence of an irregular mass lying immediately below the left lateral incisor and the left canine. This mass proved, on removal, to be an odontome, evidently an aberration of the central incisor tooth-germ, showing some attempt at a definite arrangement of the hard tissues, and, if examined more closely, serving as an illustration of calcification going on in three definite columns.

#### DISCUSSION.

The PRESIDENT remarked that these curiously misformed teeth were not uncommon in the incisor region. They often came in the neighbourhood of the two normal central incisors, and, as could be seen to-night, they took various forms. He asked whether all the normal teeth were accounted for in the patient.

Mr. LEWIN PAYNE said Mr. Turner's specimen seemed to suggest that there might be an inner denticle, around which the outer portion of the tooth was developed, and for which the term "gestant composite odontome" had been suggested. He thought it would be well if an opportunity were given to make a model of the specimen, that its original form might be preserved, and then to cut a section down the centre, so as to ascertain what its contents were.

#### **An Extreme Example (Unilateral) of the Antral Cavity extending between the Molar Roots.**

By W. W. GABELL, L.D.S.

LEFT upper first and second molars from a girl, aged 20, showing the antral cavity extending well down between the roots. Between the roots of the second molar the antrum extends 6.5 mm. ( $\frac{1}{4}$  in.) below the level of the apices. Between the roots of the first molar the antrum extends downwards for 4.5 mm., completely occupying for that distance the space (9 mm. wide at the apices) between the palatine and post-buccal roots, which act in part as its walls. On the right side the

antrum is not reached by any of the roots, and the palatine and buccal roots of the six-year molar, instead of being widespread, are joined. There was no history of antrum trouble and the wounds have healed well.

#### DISCUSSION.

Mr. W. W. GABELL said that in giving the specimen to the Museum he did not claim that there was anything very exceptional about it; it was a good example of a not uncommon condition. The antrum here went right up between the roots of the six-year molar. In looking over the papers on the subject, he found but little definite information as to where one might expect the antrum. In a paper read before the British Dental Association last year, this condition was described as fairly common. Still, on operating it was rather alarming suddenly to find one had brought away the floor of the antrum and left a large space. Here, no special treatment was required. The patient was instructed to keep the mouth and wound well cleansed with frequent rinsings, and it healed perfectly.

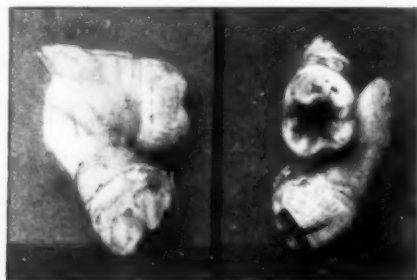
The PRESIDENT remarked that he did not see why any trouble should ensue afterwards if the parts were kept clean. Mr. Underwood, who had done recent work on antrum conditions, showed that whenever an upper molar was present the floor of the antrum was above it. If the third molar was standing, one knew that the antrum extended as far back as that. He recalled the description of the antrum in "Holden's Osteology," a favourite book in his student days, and the narration of a case in which a lady pushed up through a hole on one side most of a thin quill pen. She feared it must have penetrated her brain and consulted Highmore, who explained that the pen had turned round and round and adapted itself to the curve of the antrum.

Mr. STANLEY MUMMERY said he was interested in this specimen because a week ago he had a very similar event. He took out the second upper molar from a lady who suffered from pyorrhœa; the tooth was quite loose. A great gush of blood followed from the left nostril. He thought it better not to syringe it, but told her to come again the next day. On her return she said she had a profuse discharge of blood on arriving home, lasting a few minutes. It quieted a few days later, and healed up. The root of that tooth had obviously perforated the floor of the antrum, and was in a very septic condition, but she had no symptoms of antral trouble while the tooth was in situ.

**Fusion of Maxillary Molars.**

By G. C. BIRT, M.R.C.S., L.D.S.

MR. BIRT said this was a specimen showing fusion between the second and third left upper molars. There was no caries in the specimen, but the mouth, that of a patient, aged 41, contained chiefly decayed stumps and he was clearing it for a complete denture. Probably the third molar was slightly erupted since the fissures of its crown contained traces of tartar, but he was unaware of its presence until after



Fusion of maxillary molars.

the extraction, which was remarkably easy. On examining it one could see that the second molar was normally placed, but that the crown of the third molar was directed very much inwards and slightly backwards (an unusual direction). The roots of the two teeth were much mixed up together, but the pulp chambers were quite distinct. Probably the third molar, owing to its peculiar position and to the interlacing of the roots, was unable to erupt more than sufficient for one cusp to break the surface of the gum, thus allowing a septic pouch to form around the tooth, which sepsis caused the great proliferation of cementum which could be seen covering all the roots. This proliferation in its turn fused the interlacing roots together, producing the condition of false gemination.

The Structure of the Dental Pulp in Ovarian Teratomata.

By A. HOPEWELL-SMITH, M.R.C.S., L.D.S.

THIS short communication may be regarded in the light of a sequel to a paper<sup>1</sup> read before this Section last year by Mr. McAdam Eccles

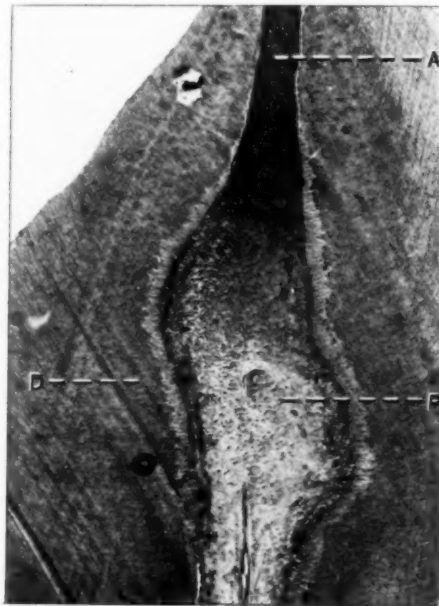


FIG. 1.

General view of pulp. D, denture; P, pulp tissue; A, coronal portion of pulp. ( $\times 45$ .)

and myself. In the discussion which then ensued Sir John Bland-Sutton expressed the opinion that it would be of some interest to ascertain whether the pulps of such teeth possessed nerves. As we

<sup>1</sup> "Dermoid Teeth or Teeth developed in Teratomata," *Proceedings*, 1911, v, p. 128.

pointed out at the time, his observations, together with those of Mr. Charters White, showed that nervous systems can be found in such bodies. It seemed, however, necessary to decide, once and for all, whether these are constant; and thanks to the kindness of Sir John Bland-Sutton in supplying me with fresh material, I am able to present a few remarks on the subject. This material is necessarily very limited in amount, and difficult to obtain, for the removal of the "teeth" for examination purposes, from the cysts, at once destroys the value, other than purely dental, of the specimens.

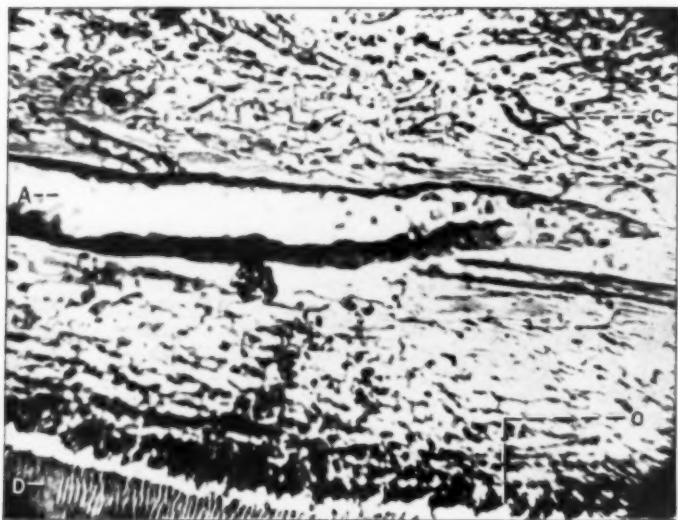


FIG. 2.

Longitudinal section of pulp. D, dentine; O, odontoblasts; A, artery; C, capillary. ( $\times 250$ .)

It is interesting to note that, in spite of the lack of special treatment by various histological reagents, at the time of the removal of the cysts, the parts are fairly well preserved by the action of formalin or alcohol, in which the whole of the soft tissues are placed. As it is impossible, however, to perfectly fix and harden the soft dental pulp, without the opening up of its containing cavity to allow of the complete penetration of the fluids, and as this has not been done, it is remarkable



that so few post-mortem changes have apparently occurred and are observable in the sections.

The specimens were prepared by rapid decalcification, and embedded in a saturated solution of dextrin, which, in certain circumstances, is more suitable than gum mucilage. They would have been ruined by employing the Koch-Weil method. After horizontal division, sections were cut on the ether freezing microtome, and stained chiefly with hæmatoxylin, for photomicrographic purposes.



FIG. 3.

Wall of pulp. D, dentine; O. Z., odontogenetic zone; O, odontoblasts; P, pulp tissue. ( $\times 250$ .)

The dimensions of the pulp are very small: in those examined it was less than 9 mm. in length, and in greatest width it did not exceed 0.75 mm. Its outline is less regular than that of the normal organ, and varies very considerably with the shape of the "tooth" itself (fig. 1). The pulps, on the whole, are composed of tissue closely resembling that in normal conditions. It is "a delicate connective tissue consisting of ramified cells embedded in a slightly fibrous stroma and granular transparent basis substance, and is plentifully supplied with blood-vessels and nerves" (fig. 2). In the coronal region it is

practically a solid mass, the basis substance being abundant (fig. 1, A). Here the cells are few, small, and have oval nuclei. The odontoblasts are inconspicuous. As the pulp increases in width the density of the structure is less noticeable, and the periphery of the soft parts is similar to that of normal teeth, although everything is on an infinitely smaller scale. The odontogenetic zone is clearly seen (fig. 3) even in decalcified sections, the dentinal processes of the odontoblasts crossing it at frequent intervals. In its youngest portions the pulp cells proper are exceedingly branched (fig. 4) or spindle-shaped, and their planiform

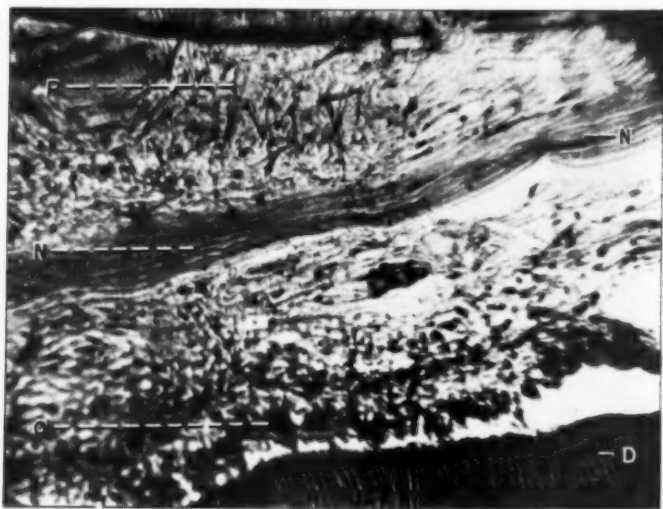


FIG. 4.

Longitudinal section of pulp. D, dentine; O, odontoblasts; P, branched pulp cells; N, bundle of large medullated nerve-fibers. ( $\times 300$ .)

nuclei are about the same size as those of the endothelial cells of the capillaries. The odontoblasts are short, thick cells about  $15\ \mu$  in length, and are often separated from one another by large spaces. In many instances their lengths and diameters are identical. All cells show degenerative changes, probably post mortem. The basal layer of Weil may be detected in places. The blood-vessels run in the same direction as the long axis of the "tooth," and are accompanied by

prominent bundles of medullated nerve-fibres, which appear to be fewer in number than elsewhere. An outstanding feature of the sections is that these nerve-fibres, when compared with the dimensions of the soft parts, are very much larger in proportion than those of adult teeth (figs. 4 and 5).

It may reasonably be assumed that the nerves in ovarian dental pulps cannot exist for any other than trophic purposes. In assigning a rôle to the odontoblasts, however, the same difficulties arise as with these cells in normal conditions, unless it be granted that the dentinal



FIG. 5.

Similar to last figure. D, dentine; O, odontoblasts; B, blood-vessel cut transversely; N, nerve bundles. ( $\times 280$ .)

fibrils, which are part and parcel of these cells, and obviously pass into the dentinal tubes, are trophic for the dentine, and do not perform, in ovarian "teeth," the dual function of those situated in the oral cavity.

Whereas a skiagram is of great value in assisting the diagnosis of ovarian teratomata in the living state, the age of the cyst can be approximately determined by the presence, or otherwise, of the dento-genetic zone. If it is seen in either longitudinal or transverse sections

it may be surmised, as a matter of clinical interest, that the cyst is of fairly recent origin, or at all events the accidental dental tissues have been quite recently developed.

#### DISCUSSION.

The PRESIDENT said Mr. Hopewell-Smith's investigations were extremely interesting. He seemed to have concluded that the nerves there served only a trophic purpose. He (the speaker) did not see why there should be any trouble about that; and he would have expected the nerves there to carry out the same function as nerves elsewhere. He did not think that Mr. Hopewell-Smith had shown that the nerves he had described differed from those in ordinary tooth pulp.

Mr. HOPEWELL-SMITH replied that there was great difficulty in finding nerves in dentine, and in ovarian teratomata there was very little material to work upon. One could only find medullated nerve-fibres in the pulp.

## Odontological Section.

June 23, 1913.<sup>1</sup>

Mr. P. SIDNEY SPOKES, President of the Section, in the Chair.

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### PRESIDENT'S VALEDICTORY ADDRESS.

GENTLEMEN,—As our meetings will now be suspended until October, when your new President takes office, this is the occasion upon which I must detain you for a short time with a valedictory address to review our year's work.

At the November meeting we were again indebted to Mr. Howard Mummery who brought us a fortunate section showing a nerve-bundle with its brush-like expansion cut on the same plane as the dentinal tubes, whereby it was possible to follow the course of the neurofibrils into the dentine. The discussion introduced by Mr. Badcock upon "Modern Orthodontics" was marked by the expression of diverse opinions, as was to be expected. Although the session was prolonged it was found that there were yet other warriors ready to take the field, and the following meeting was therefore devoted to a continuance of the discussion. Not only was there no consensus of opinion forthcoming as to the causation of irregularities of the teeth, but the result of the conflict as to treatment possibly left the silent members content to hold the view that at present no arbitrary rules are applicable or justifiable for the treatment of every case of mal-occlusion of teeth. Nevertheless the debate was ably maintained, and if it resulted in further formulating the ideas of opposing schools must be credited with usefulness. Mr. Berwick read a paper upon the construction of apparatus for use in congenital defects and for restoration after surgical operations upon the jaws. The subject was dealt with in a practical manner, and produced a good discussion.

<sup>1</sup> Meeting held at the Royal College of Surgeons.

Another paper was by Mr. J. G. Turner on "The Preparation of the Mouth before Operation," and was marked by the originality, thoroughness, and forcible diction which, by experience, we have become accustomed to expect from Mr. Turner. Here, again, a good discussion followed and, incidentally, there was an exchange of opinions upon the question of local anæsthesia. We were also indebted to Mr. Shiach for giving the Section an opportunity of learning the details of the life-history of a remarkable man—James Gordon, of Bristol—and of seeing some of the marvellous carvings which he did.

Then in April we had a discourse by Professor Keith upon "Dental Problems in Prehistoric Man," which apart from its interest at the time will, in its printed form, afford a valuable means of reference to those interested in palæontology. We were introduced to some new terms suggested by Professor Keith to distinguish the Neanderthal type of molar from the simian and human. In the former there is a tendency for the body of the tooth to enlarge at the expense of the roots, and instead of the name *hypsodont* with which we are all familiar, but which Professor Keith considers is not applicable, the term "*taurodont*" is suggested in distinction to the opposite condition "*cynodont*," or, as we should say, *brachyodont*. At the same meeting Mr. Warwick James showed and described a simple apparatus for the prevention of mouth-breathing, and at our last session this was discussed by other members who have had the opportunity of trying it with success. Mr. Hopewell-Smith's welcome paper on the "Dental Histology in Teratoma" will be fresh in your memories.

Several special sessions of the Royal Society of Medicine were given up to a general discussion upon the subject of "Alimentary Toxæmia." The oral sepsis factor naturally attracted members of our Section and half-a-dozen made contributions. It is perhaps with the views expressed as to treatment of pyorrhœa that we are most interested and, as is well known, very divergent opinions obtain on this question. On the one hand, it seems to be insisted that when it is possible to demonstrate even a moderate degree of separation between gum and tooth the patient is in jeopardy, and that if there be no actual pyorrhœa present yet the probability in some mouths of stagnation areas resulting in infection is so great that the removal of teeth is therefore considered not only justifiable but imperative. On the other hand, the extraction of all the teeth in a young adult suffering from a mild degree of pyorrhœa, with perhaps a quarter of the alveolar margin of the tooth-sockets lost, is held to be an unwarrantable and barbarous proceeding

and hardly in keeping with recent advance in modern surgery. Here the treatment advocated is immunization by vaccines accompanied by local surgical measures; but some are so anxious for conservative treatment that they resort to splints and other means intended to give rest to very loose teeth whilst other treatment is carried out. For the purpose of comparison I have put the terminals widely apart, and have somewhat broadly stated what may be considered the extremes. I would venture to urge that those who prefer to take a middle course must not be charged with obstinacy, ignorance, or inability to understand the value of evidence. They claim that each case should be considered on its own merits; age, physical conditions, personal, and even family, history receiving attention. It is easy to decide between forceps and splint, but there are opportunities in a large number of cases for the exercise of judgment based upon experience, and these are precisely the ones in which it is wiser not to subscribe to a routine method.

The "Casual Communication" is always a feature of interest, and we are indebted to several members for valuable contributions during the year.

In conclusion, I have to thank not only the members of the Section for allowing me to occupy the position of President, but also the Council for their assistance and indulgence during my term of office. To the two Secretaries formal words are quite inadequate to convey my sense of indebtedness, for to them is due whatever of success there has been in Council and Section arrangements.

### **Model showing Large Maxillary Incisors.**

By A. E. BAKER, M.R.C.S., L.D.S.

MODEL of upper teeth of a boy, aged 9 or 10, of stunted growth (taken three years ago by Mr. A. J. Baker, of Portsmouth). It shows the central incisors partially erupted and abnormally large, their combined width measuring  $1\frac{1}{16}$  in.; whereas the combined width taken from a series of models of normal upper central incisors is given as  $\frac{5}{8}$  in. Unfortunately the case has been lost sight of as no treatment was undertaken.



**Some Recent Additions to the Odontological Collection of  
the Royal College of Surgeons Museum.**

By J. F. COLYER, M.R.C.S., L.D.S.

THIS evening I propose to bring before the Society a few specimens of more than usual interest which have been added to the Odontological Collection during the last three years.

**INJURIES TO THE JAWS AND TEETH.**

The first specimen to which attention may be directed is a very fine skull of a lion, an uncaptured animal. In the course of combat the

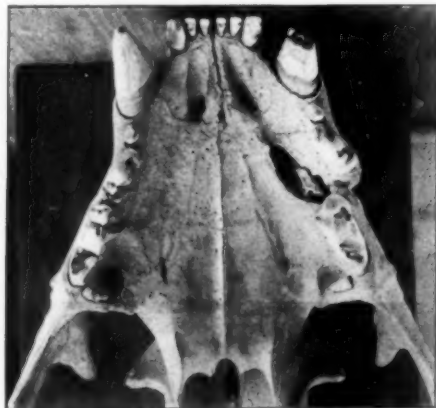


FIG. 1.

animal must have received an upward thrust from his opponent, in the left maxilla. The effect of the blow was to fracture the bone and displace it in an upward and forward direction. The line of fracture starts from the anterior palatine foramen and runs backwards and outwards to the interval between the third and fourth premolars (fig. 1). From here it passes upwards and slightly backwards, the line of fracture being just in front of the infra-orbital foramen (fig. 2). The effect

of the displacement was to crumple up the nasal bone (fig. 3). An examination of the specimen does not lead one to think that any marked degree of suppuration followed the injury, and as far as one can judge the animal lived for a considerable period after the injury. The specimen



FIG. 2.



FIG. 3.

is interesting inasmuch as it demonstrates how animals in the wild state may receive severe injuries and recover completely from the effects.

Another specimen illustrating the effects on the permanent teeth of injury to the deciduous teeth is shown in the skull of a leopard (fig. 4). The maxillary deciduous canines have been injured so as to lead to exposure of the pulp cavities and subsequent death of the pulp. The

effect on the growing permanent canines is well seen. The injury would seem to have completely disorganized the growing end of the tooth, with the result that growth ceased, with the formation of an irregular mass of tissue. The teeth, by this means stunted in their growth, have



FIG. 4.

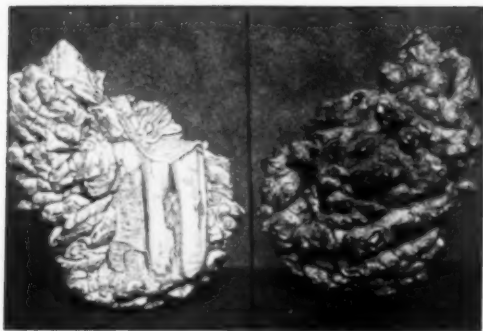


FIG. 5.

remained unerupted. Injuries of this character to the canines of the carnivora are comparatively common, and the resulting condition in the permanent teeth seems to shed a ray of light on those curious aborted premolars occasionally met with in the human subject, suggesting that these malformed teeth are probably the result of injury received during the extraction of their deciduous predecessors.

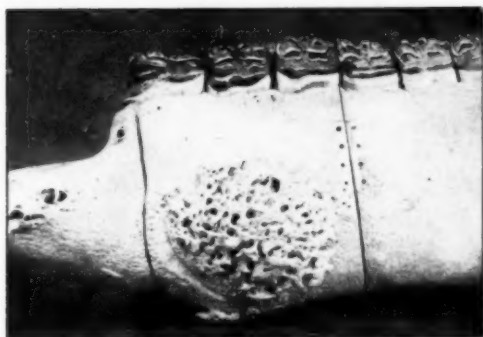


FIG. 6.

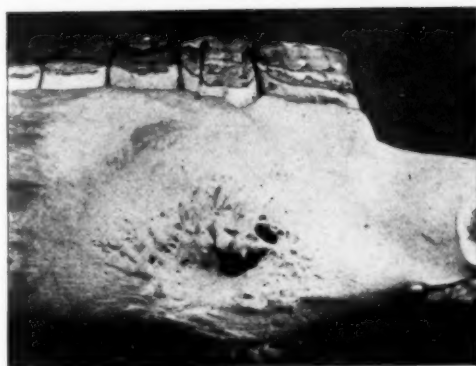


FIG. 7.

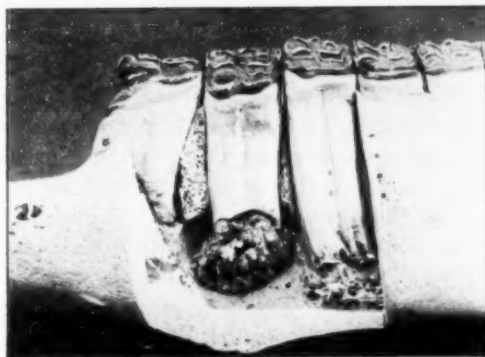


FIG. 8.

## ODONTOMES.

A good example of a radicular odontome in a sheep is shown in fig. 5. This specimen was picked up on a sheep run in New Zealand and was presented to the Museum by Mr. William Smale.

Another interesting specimen is shown in fig. 6. It is a portion of the mandible of a horse. The body of the bone is considerably thickened and presents on the outer surface a sponge-like appearance (fig. 7), while on the inner aspect there is a well-marked sinus leading into the body of the bone. The teeth appear to be quite normal, there is no caries and no sign of periodontal disease. On removing a portion

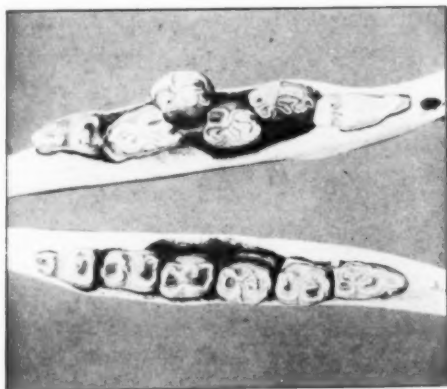


FIG. 8A.

of the outer layer of bone the condition shown in fig. 8 was discovered. Around the end of the third premolar there is a cauliflower-like growth of very fragile consistency. This growth is situated in a definite cavity; the outline of which is in places globular and the surface smooth, suggesting that it had been lined with a thickened tooth capsule. The specimen seemed to suggest an odontome around which suppuration had taken place. On raising the tooth so as to expose the inner aspect of the socket, a smooth groove was observed running from the gingival margin to the apical portion of the tooth, and on replacing the tooth it was found to form with the latter a definite canal. Whether this canal was occupied by blood-vessels or tissue of another character it is impossible to state, but there is, I think, little doubt that the infection to the apex of the tooth travelled via the abnormal canal.

## PERIODONTAL DISEASE.

Several specimens have been added to the collection of animals showing periodontal disease. Of these mention may be made of two kangaroos and a horse (fig. 8A), showing stages of the disease not previously represented. With the addition of these specimens the collection now contains a gradational series from the earliest to the most advanced stage.

With a view to enhancing the value of the specimens an endeavour is being made to add skiagrams of the teeth and jaws in cases of periodontal disease in man. An example is shown in fig. 9. The teeth

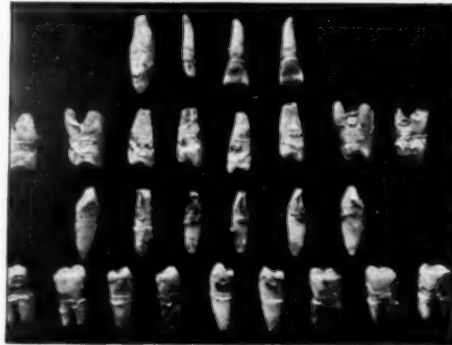


FIG. 9.

were removed from a man of just under fifty years of age. They show the characteristic appearance seen in these cases—namely, marked absorption of the apical portion of the teeth, with adherent masses of adventitious tissue between the clefts of the molar roots. The skiagrams of these teeth show the extent of the bone destruction and the rarefying osteitis around the apical portion of the majority of the teeth (figs. 10 to 12).

## IRREGULARITIES OF THE TEETH.

A valuable specimen of irregularity of the teeth in a horse has been added to the collection. There is a general crowding of the premolars on the right side of the maxilla accompanied by a twisting

to that side of the front part of the bone. The crowding is due to a deficiency in growth of the right maxilla. Taking the canals on the palatine aspect as points for measurement, the distance on the normal side is  $6\frac{1}{4}$  in., on the defective side,  $5\frac{1}{2}$  in. An examination of the facial surface reveals a similar difference.

A good example of protrusion of the upper teeth in a horse ("parrot mouth") is another specimen worthy of notice. In the horse the upper and lower second premolars meet flush, in the specimen showing protrusion the maxillary teeth occlude in advance of the normal. Com-

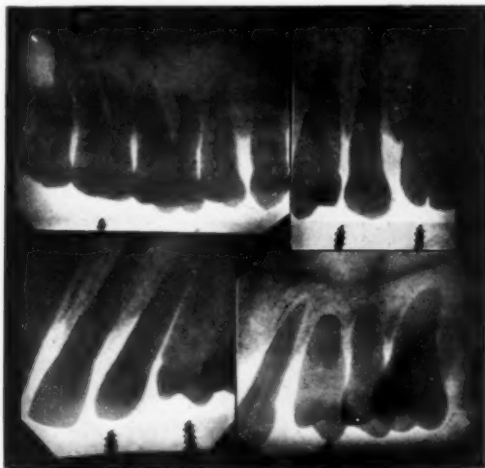


FIG. 10.

parative measurement of this specimen with normal skulls does not lend support to the view often held, that the deformity arises from lack of development of the mandible, but rather goes to show that the trouble in a great measure lies in an overgrowth of the premaxillæ.

In animals possessing teeth of persistent growth one often meets with specimens where the teeth have assumed an abnormal direction. In the hippopotamus the mandibular canines should grow in an upward and slightly backward direction and meet the opposing teeth, the attrition of the opposing teeth keeping the terminal portions chisel-shaped and therefore useful weapons in combat. In the skull shown in fig. 13, the mandibular canines have forsaken their normal course and have



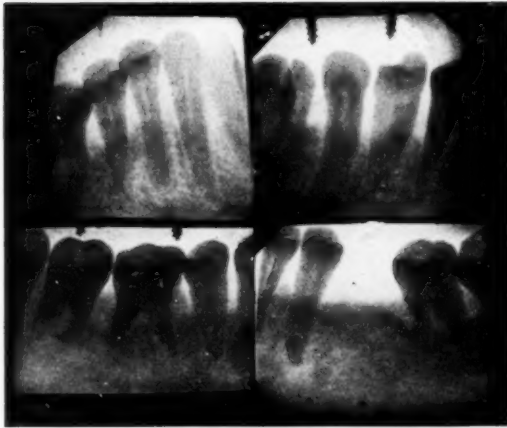


FIG. 11.

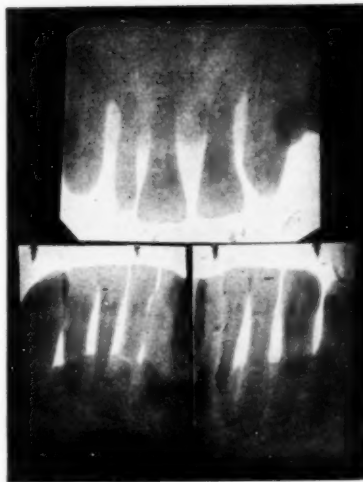


FIG. 12.

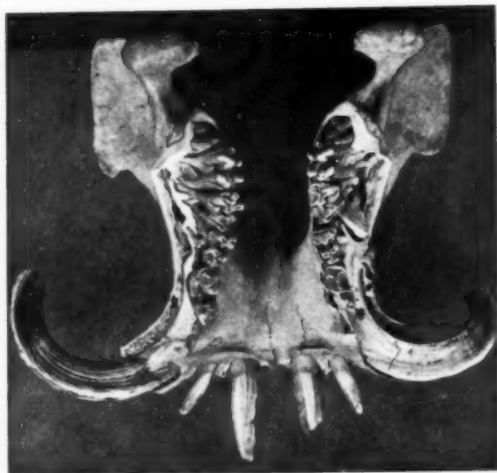


FIG. 13.



FIG. 14.

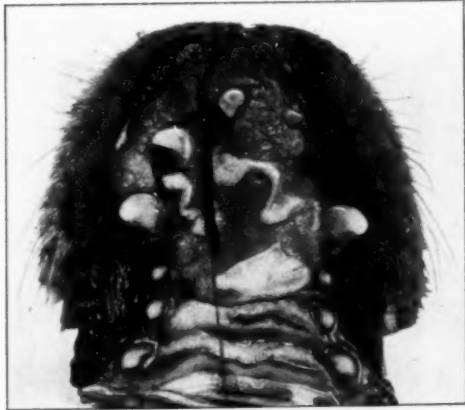


FIG. 15.

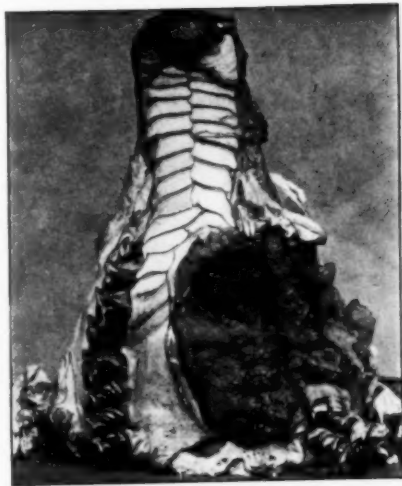


FIG. 16.

150 Colyer: *Recent Additions to Odontological Collection*

taken a horizontal direction. In investigating this specimen I noticed a curious projection in the neighbourhood of the mental foramen, and with a natural inquisitiveness I was tempted to remove the outer layer

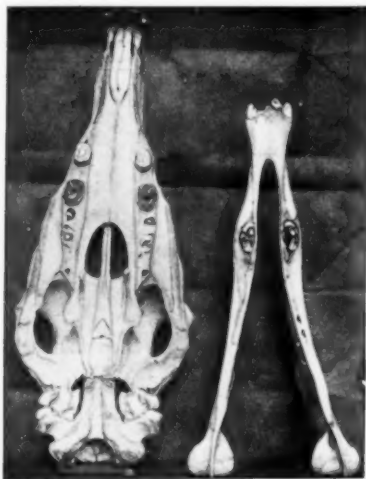


FIG. 17.



FIG. 18.

of bone. This brought to light a most remarkable condition. Overlying the tusk in the region of the mental foramen there were the cone-shaped denticles, to all appearances aborted incisors. Towards

the end of the root there was an irregular dumpling-shaped mass of tooth tissue which proved to be three, if not four, of these cone-shaped denticles fused together (fig. 14). On the right side of the specimen no denticles were found.

#### TUMOURS IN ANIMALS.

An example of a fibrosarcoma of the jaw in a dog intimately associated with sepsis around the incisor teeth is shown in fig. 15.

A skull of a Markhoor exhibiting extensive destruction of the right maxilla from a carcinoma is shown in fig. 16.

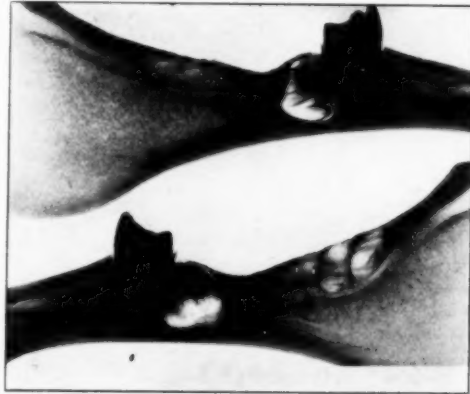


FIG. 19.

#### ARREST OF DEVELOPMENT OF TEETH IN A HORSE.

The last specimen I propose to refer to is a remarkable example of arrest of growth of the teeth in a foal. The dentition of this animal is represented as follows:—

(1) In each premaxilla there are two incisors, abnormal in shape. The cutting edges, instead of presenting a straight line, show a central well-marked cusp, with ill-developed cusps on either side. Skiagrams show that the third deciduous incisor and the permanent incisors are absent.

(2) In each maxilla there are two malformed teeth and three crypts. Two of the crypts contain aborted teeth. There are no signs of

permanent teeth. The shape of the erupted teeth is shown in figs. 17 and 18.

(3) In each half of the mandible there are two malformed incisors, one erupted premolar. Immediately posterior to the premolar and embedded in the jaw is an aborted tooth, then follows an interval free from teeth and then a crypt containing a small denticle.

Unfortunately, I have been unable to obtain any history of this specimen. Fig. 19 is a skiagram of the mandible.

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OF THE  
ROYAL SOCIETY OF MEDICINE

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VOLUME THE SIXTH

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COMPRISING THE REPORT OF THE PROCEEDINGS FOR THE  
SESSION 1912-13

SECTION OF OPHTHALMOLOGY



LONDON  
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## SECTIONS OF NEUROLOGY AND OPHTHALMOLOGY

(Combined Meeting).

(NOTE.—This portion is independently paged in Roman numerals so that it may be bound at the end either of the Neurological Section or of the Section of Ophthalmology.)

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The Council think it right to state that the Society does not hold itself in any way responsible for the statements made or the views put forward in the various papers.

## Section of Ophthalmology.

November 6, 1912.

SIR ANDERSON CRITCHETT, Bt., C.V.O., President of the Section,  
in the Chair.

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### A Case of Sarcoma of the Choroid of Unusual Chronicity.

By E. NETTLESHIP, F.R.C.S., F.R.S.

THE clinical history of this case extends from the winter of 1885-86, when the first symptom was noticed, to 1911, when the eye was excised, about twenty-six years. Mr. Lawford should by right narrate it as the patient was in his hands for the operation, but has been kind enough to say that I am to do so as I saw the case in its earliest stage.

Dr. X. (P. 12, 233) was sent to me by my late colleague, Dr. Ord, on June 15, 1886, aged 51. On taking to glasses the previous winter he had found that sight was not the same in the left eye as in the right. I found vision of right  $\frac{6}{6}$  promptly, refraction emmetropic, 1 J. p.p. about 11 in., fundus normal; left  $\frac{6}{6}$  after careful looking, improved by  $-0.5D$ . cyl., 1 J. not so well as right, and p.p. decidedly a couple of inches farther off than right, lens very carefully examined and free from visible changes, fundus normal. He said he had had syphilis thirty years previously, and I therefore particularly noted the pupils and found them equal and active both to light and accommodation; T. was normal in each. I recorded fundus normal in each, but as no mydriatic was used the record cannot be taken as conclusive, and probably a slight degree of the change seen on the next occasion was already present. I dismissed him with a slight alteration in his glasses. I noted his hair colour as "light," but did not record the iris colour; the iris of his remaining eye is light, bluish-grey, and he now tells us, in reply to a question, that the other iris always had exactly the same colour.

He came again on October 20, 1887 (interval, sixteen months), with right  $\frac{6}{6}$  as before; but left only  $\frac{6}{12}$  or  $\frac{6}{9}$ , and he said that print looked "crooked and squeezed up," vision better, with  $+0.5D$ . cyl., but

## 2 Nettlehip: *Sarcoma of Choroid of Unusual Chronicity*

not  $\frac{6}{9}$ . On dilating the left pupil I now found just below the Y.S. a somewhat oval area of altered choroid, consisting of a dark centre surrounded by a pale zone. The dark part had a uniform dull, greyish-black colour with soft edges passing gradually into the pale belt, the latter being apparently due simply to absence of the pigmented epithelium. I did not measure this smudgy-looking, dusky area in terms of the optic disk, but noted it as "large," and made a rough diagram showing it quite as large as the optic disk, or say, 1.5 to 2 mm. in diameter.

Two years after the above note (October, 1889) there was little if any change, the soot-like, smudgy centre and pale zone having the same appearance, and not looking decidedly larger than before; the patch did not appear to be raised, and the retinal vessels passed undeviated and unobscured over it. He had complained in 1887 of positive coloured scotomata, but now was not troubled by them, and said sight had improved: the micropsia, however, was still present. We then lost sight of him for seventeen years, when, in October, 1906, he consulted Mr. Richardson Cross.

Mr. Cross found that with +1.5 s.  $\ominus$  -0.75 c., vision of the affected eye was still  $\frac{6}{9}$ , but there were again some subjective visual sensations, and now the upper part of the field was impaired, and a reddish-grey rounded mass was seen with +10D., suggestive of sarcoma. November, 1907, "better," having lost the subjective sensations, but vision reduced to  $\frac{6}{18}$ . February, 1908, vision only  $\frac{6}{36}$ , the localized mass, two or three optic disk diameters, seen with +10D. much as before, and not pigmented; eye perfectly comfortable.

On July 12, 1911, when Mr. Lawford saw him, the eye had become glaucomatous with moderate congestion, dilated, fixed pupil, and steamy cornea, the fundus reflex grey in lower part, dull red above; nothing could be focused behind the lens. Eye excised on July 15, 1911.

Mr. Cyril Hudson reports as follows upon the specimen: In the lower half of the eyeball is a globular white growth about the size of a small cherry situated to the temporal side of the optic disk, and attached by a neck, 2.5 mm. or 3 mm. thick, to a thin lens-shaped base in the choroid measuring about 7.5 mm. in diameter. Greatest height or thickness of tumour 9 to 10 mm.; distance of most prominent part from back of lens, 6 mm. Retina extensively detached in same part of eye. Microscopical sections show that the tumour is unpigmented, composed of short spindle cells, and contains many irregular blood-channels, most of which have a considerable amount of



homogeneous-looking connective tissue in their walls; the growth has extended up to the edge of the optic disk, and into the sclera, along one of the posterior ciliary arteries. Retina detached up to ora serrata. Angle of anterior chamber cut off on nasal side by attachment of periphery of iris to Descemet's membrane; some loose cellular tissue in angle at opposite side.

I do not think it occurred to me when I saw the patch of choroidal disease of unusual aspect in 1886 to 1889 that it might be an incipient tumour. I ought, however, to have suspected that something active was going on at the patient's second and third visits (1887 and 1889), not because the choroidal spot looked like a growth, for it did not, but on account of the metamorphopsia and micropsia of which the patient complained in that eye. He was a valetudinarian, not a busy man, and paid much attention to his symptoms, and I suppose all this led me to treat the case lightly. In fact, I classed it with a few others I had occasionally seen in which there was nothing unnatural in the choroid except a single patch or spot of dusky, or greyish-black, or slaty colour, shading off into the normal, usually discovered during routine examination and generally causing no symptoms; the appearance reminding me more of a small smudge made by black crayon or soot than anything else, and being perhaps congenital.

The first case of this smudge mark in the choroid that I find careful notes of was in a man aged 58 (Case 2), whom I saw at hospital in 1875 (P. 2, 49). A little below and to temporal side of Y.S. in the left eye was a small patch about one-third the area of the disk, of dusky discoloration of the choroid, quite definite, but merging gradually into the healthy structure around and looking "as if the choroid here had been smudged with a sooty mark"; a retinal vein crossed the patch unobscured. He came for a "fog" before this eye noticed a few days before, but neither eye saw perfectly, and the general defect of sight may have been due to tobacco. Four months and a half later the patch looked exactly the same.

*Case 3.*—In the next case the patch increased considerably in diameter during the five months and a half it was under notice, and the retina over it showed changes. I thought it was a sarcoma and should have much liked to know what happened. Miss A., aged 46 (P. 21, 23), from Wales, July 4, 1890: Vision  $\frac{6}{60}$  with each, Hm. 0.5D., requires +2D. In right a "sooty" choroidal patch just below and rather larger than the optic disk; not sensibly swollen, edge fairly defined, but soft or shading off into the normal, some scattered whitish stippling in the overlying retina, but a retinal vessel runs unobscured over the patch. It causes no symptoms. December 18 (interval five and a half months): Vision still  $\frac{6}{60}$  with each eye, right patch now

#### 4 Nettle-ship: *Sarcoma of Choroid of Unusual Chronicity*

measures three or four times the area of the disk, and the retina over it shows numerous small, white spots; surface of patch seen with +1.5, but the surrounding parts of fundus have almost or quite the same refraction. No later note.

*Case 4.*—Mr. X., aged 64 (P. 19, 20), August, 1889. Right above Y.S. area and crossed by superior macular vessel a "sooty" patch equal in area to optic disk. Some chocolate-coloured hæmorrhage at inner part of fundus, opacities in vitreous, and a large patch of old pigmented choroiditis in lower part of fundus. The hæmorrhage had disappeared two months later, but the "sooty" patch was unaltered.

*Case 5.*—In another, a lady, aged 51 (P. 26, 78), with syphilitic retinitis and hyalitis of both eyes, but no conspicuous choroidal changes, the "sooty" patch, which was about twice the area of optic disk, and situated to the upper temporal side of Y.S., when first seen in the early stage of the constitutional disease, had exactly the same appearance six years later, although characteristic ups and downs had occurred in the retinal disease during that time.

*Case 6.*—In another lady, a widow, aged 50 (P. 26, 74), the patch measuring about one-quarter of the optic disk area and seated to the nasal side of optic disk, did not alter during the two months it was under notice. She also was suffering from mild double syphilitic retino-hyalitis.

*Case 7.*—An old gentleman, aged 79, with diabetic retinitis in each eye, had a rounded patch of this smudgy black choroidal abnormality in the right, crossed by the superior temporal artery, and about as large as the optic disk. Nine months later the details of the retinitis, indicated as before in my notes by a rough sketch, had altered; nothing is now said about the choroidal patch, but the examination was so careful that I could scarcely have failed to notice an alteration, had any occurred.

I have records of some ten other cases, making, with the above half dozen, sixteen, from notes of private patients in about twenty-five years. In only seven—viz., the case of proved tumour forming the main subject of this paper, and the five cases just briefly related (numbered 2, 3, 4, 5, 6, 7, above)—was the appearance of the patch recorded a second time. In Case 3 it had increased decidedly in between five and six months, but what happened after that I do not know; in Case 5 it altered not at all in six years, nor in Case 7 in nine months; in the other three (Cases 2, 4 and 6) the interval between first and second examinations was too brief to be of much value.

The patch was situated close to the fovea, and the eye free from any other changes, in two cases, Case 1 (the tumour case) and Case 2, and these were the only two in which complaint was made of defective vision that could fairly be attributed to the choroidal patch. The patch was in the macular area in six others (Cases 4, 5, 9, 7, 12, 13 of my

list), but so far from the fovea that any defect of vision it might cause could readily pass undetected by the patient, especially as in several of them (Cases 4, 5, 7, 13) there were other and more extensive changes causing lowered vision, either in lens, vitreous, or retinae. In the remaining eight cases (Nos. 3, 8, 6, 10, 11, 14, 15, 16) the smudgy spot was quite away from the macular region, usually near the optic disk, above, below, or to nasal side, and once at the equator. I have no record of ever seeing such a patch at the periphery, and although that may be because the peripheral parts of the fundus seldom receive the same attention as the central area, it is a fact that in at least six of the published specimens of minute sarcoma discovered accidentally post mortem, and referred to further on, the tumour was in the central region; in only one was it as far forward as the equator. Statistics of operated cases of choroidal sarcoma often show that the posterior (central) area is more liable than the equator and anterior parts (Parsons, quoting Fuchs). I have no doubt I have overlooked a good many of the smudge patches I have been alluding to at one or another part of the fundus, especially as they are often less easily seen by direct than indirect examination, and the decreasing employment of the indirect method of late years would favour their escaping detection.

The suggestion I make is that these clinical cases of choroidal smudge spot, or some of them, may be the counterparts of certain specimens of minute sarcoma of choroid that have been found accidentally post mortem, and that will be referred to immediately. Others of them are probably congenital<sup>1</sup> and stationary, and in this connexion it may be noted that in one of my patients (No. 12), a man, aged 47, in whom both irides were light brown, there were darker brown spots on the iris of the eye containing the choroidal spot, but no spots on the other iris. The condition I am describing has, I need hardly say, no ophthalmoscopic resemblance whatever to Stephenson's congenital pigment spots in the retina.<sup>2</sup>

It will be observed that in the case forming the foundation of the present paper there appeared to be disturbance of the pigment epithelium when the patch was first seen, while in the only other strongly suspicious case (No. 3) the retina lying over the patch showed decided white stippling. Probably such visible disturbances are proof that the choroidal patch is growing and not a stationary congenital affair,

<sup>1</sup> Purtscher, quoted by Parsons, "The Pathology of the Eye," 1905, ii, part ii, p. 519.

Stephenson, Sydney, *Trans. Ophthal. Soc.*, 1891, xi, p. 77.

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and in support of this we observe that the pigment epithelium was disturbed in the first of Fuchs's second group of cases<sup>1</sup> and both epithelium and outer layers of retina were altered in a similar, but larger, sarcoma, published by myself in 1902.<sup>2</sup> Some opacity of retina and disturbance of pigment at the margin is mentioned also by Kipp,<sup>3</sup> in his case (1905) where the tumour, situated just below the Y.S., was but little larger than the optic disk when the eye was removed; but in this case the whole process was relatively acute.

The first recorded case of minute sarcoma of the choroid is, I believe, the one of which sections were shown by Fuchs at the Heidelberg Congress in 1900 (*Bericht*, 1900, p. 197). The patient, a woman, aged 34, had died of diabetes, and diabetic retinitis had been diagnosed by ophthalmoscopic examination. The detailed clinical notes had been mislaid, but the microscopical appearances were fully described, and in Parsons's "Pathology of the Eye," vol. ii, p. 518, fig. 376 is taken from one of Professor Fuchs's sections of this specimen. In this case Fuchs particularly states that the elastic lamina and pigment epithelium were normal on all parts of the specimen (*loc. cit.*, p. 197, bottom line).

In the discussion on the above specimen, Wintersteiner (*ibid.*, p. 199) said he had twice come across a minute sarcoma of choroid, in one case pigmented, in the other not, measuring scarcely 4 mm. to 5 mm. in the longest diameter and not 0.5 mm. thick; both were in eyes lately operated on for cataract.

At the meeting of the American Ophthalmological Society in 1905, when Kipp described his case above mentioned, De Schweinitz and Shumway<sup>4</sup> recorded (1) a minute melanoma of choroid, area 1.2 mm. by 0.5 mm., discovered at the post-mortem examination of a negro woman, who died, aged 32, of fibro-sarcoma of brain; and (2) a second case in which a melanotic sarcoma of choroid was found post mortem in the eye of a white man who died, aged 47, of inoperable endo-thelioma of the dura mater; the choroidal growth measured 4.4 mm. in diameter and 0.9 mm. thick. In the first of these two cases the growth was 3 mm. and in the second 5 mm. from optic disk. It seems possible that in both these cases the choroidal growth was secondary to the intracranial tumours; but, even if that be so, it

<sup>1</sup> Fuchs, *Trans. Amer. Ophthal. Soc.*, 1911, xii, p. 787, fig. 4.

<sup>2</sup> Nettleship, *Roy. Lond. Ophthal. Hosp. Reports*, 1902, xv, p. 124.

<sup>3</sup> Kipp, *Trans. Amer. Ophthal. Soc.*, 1905, x, p. 437, Case 2.

<sup>4</sup> De Schweinitz and Shumway, *Trans. Amer. Ophthal. Soc.*, 1905, x, p. 439.

does not detract from the importance of watching for the earliest ophthalmoscopic changes in choroidal growths.

At the meeting of the American Ophthalmological Society in 1911, Fuchs described three other similar specimens.<sup>1</sup> The first (already mentioned above) from a man who died, aged 26, from cysticercus in the brain, was near the fovea, and measured only about 0.75 mm. in each diameter and 0.15 mm. in thickness, and was very little pigmented; the illustration (fig. 4 in Fuchs's communication) shows spacing of the pigment epithelium over the central part of the growth, but no alteration of the bacillary layer (low power drawing only). The second specimen was found in an eye excised for glaucoma from a woman, aged 67; seated at the nasal margin of optic disk, vertical diameter 1.25 mm., horizontal 1.5 mm., thickness of choroid and tumour together not more than 0.9 mm.; growth much pigmented. The third was in an eye excised for suppurative of cornea after injury, in a man, aged 37; situated in horizontal meridian rather behind equator on temporal side; horizontal diameter 2.25 mm., vertical about 1 mm., thickness of growth 0.25 mm.; no pigment except a focus of pigmented spindle cells at centre of growth; choriocapillaris and pigmented epithelium normal over the sarcoma.

Ginsburg,<sup>2</sup> quoted in the *Ophthalmic Review*, also showed in 1911 sections of a minute sarcoma of choroid, less than 1 mm. in any direction, that he had found in the eyeball of a man, aged 36.

Thus, during the last decade nine cases have been recorded (or ten if Purtscher's case be included) in which a minimal sarcomatous growth has been discovered accidentally in the examination of an eyeball after death, and also one case where the rather rapid increase of the small and uncomplicated patch at the fundus led the surgeon, Kipp, to remove the globe.

In respect to the clinical side of the subject—the diagnosis of choroidal growths at a very early stage—it is evidently important to watch over as long a period as possible any case in which a solitary spot, or patch, of dusky colour, free from signs of inflammation past or present, is seen in the choroid; for although some, perhaps a majority, of such patches may be not only congenital but likely to stay as they are, others, whether starting on a congenital basis or not, will prove to have been incipient sarcoma.

<sup>1</sup> Fuchs, loc. cit.

<sup>2</sup> Ginsburg, at the Berlin Ophthalmic Society, March 9, 1911; *Ophthal. Rev.*, 1911, xxx, p. 159.

### A Pedigree of Leber's Disease.

By E. NETTLESHIP, F.R.C.S., and A. HUGH THOMPSON, B.C.

PART of the following pedigree was recorded in the Bowman Lecture for 1909.<sup>1</sup> The family was rediscovered by one of us (A. H. Thompson) early in 1912, and has since been jointly investigated by both of us, the result being the addition of three fresh cases of the disease and much additional relevant detail.

The following are the salient points in the case: (1) The disease is known to have occurred in three generations, and is suspected in a still earlier one—the first; (2) its occurrence in females; (3) the one affected female (II, 3) who married transmitted the disease to *all* her sons (except one who died long before he reached the susceptible age), and to one of her two daughters, whilst the other daughter was a carrier; (4) excessive infantile mortality in the issue of the only affected male (III, 7) who had a very large family; (5) a mild attack followed by recovery, apparently complete, in two cases (III, 4 and 8), and substantial improvement in another (IV, 4); (6) failure of sight of unknown character in a female (IV, 1), who died of diabetes, and was a member of an affected sibship; (7) only a few of the males in the youngest generation (V) have at present reached the susceptible age; (8) most of the affected ones have lived to a good age—only two of them dying under 60—one of these deaths being from cancer. Some of these points must be spoken of in more detail.

Of the females marked as affected, II, 3, became nearly blind between 20 and 30, but whether before marriage or after is not known; she is said not to have recovered. Her one sister kept good sight, but her two brothers were affected like herself, and it is said at about the same age. One of her two daughters (III, 4) suffered from failure of vision lasting some months at least, when 14 or 15 years old, but got quite well, and remained so; two of her affected brothers gave, at different dates, almost exactly the same account of this attack, which was evidently not mere accommodative weakness, and we may conclude that this girl had the genuine disease, and recovered. Two females in I are marked with a + inside the circle (⊕); the sight of one of them

<sup>1</sup> *Trans. Ophthalm. Soc.*, 1909, xxix, p. 73, fig. 142.



(I, 2) failed when she was aged about 30, say one hundred years ago, whether before or after marriage is not certain; an operation of some kind was done upon her eyes, and she is said to have become quite blind, and remained so; she lived to be 80; she may have been operated on for supposed cataract—clear lenses have been removed even since that date! As to her sister (I, 3), the evidence is inconclusive: one nephew said she had bad vision, but no one else had heard of it; her two sons, however, certainly had the disease, and she must therefore have been either a carrier or actually affected. It is interesting that II, 3, transmitted to *all* her children (excepting the first, who died in infancy), for the only one, the daughter (III, 3), who did not show the disease carried it to her two sons. This phenomenon, a woman who manifests the disease, transmitting it to a larger proportion of her offspring, including some of her daughters, than a woman who only carries the malady without showing it, has been observed before.<sup>1</sup> The high mortality in the offspring of the affected father (III, 7) may be compared, or contrasted, with the condition in Gould's case and Menteith Ogilvie's case,<sup>2</sup> where a high infantile death-rate occurred in at least three affected sibships borne by mothers who carried, but did not display, the disease. The other affected persons in the present pedigree—besides III, 7—did not have very large families, and no history could be obtained of stillbirths or miscarriages in any of them. In V, however, not only are there several deaths marked as aged under 1 year, but some others that died in childhood above 1 year, for which reference must be made to the description of the pedigree.

The history of this pedigree is known well enough to warrant conclusions as to the course of the disease in all the cases except II, 5 and 6, III, 9, and the two doubtful ones in I. In II, 1, 2, and 3, III, 5, 6, and 7, and IV, 2, there was no recovery, or at best only a slight doubtful improvement; but III, 4 and 8, affected at an earlier age than any of the others, recovered completely; whilst in IV, 4, attacked at 28, sight improved very much about a year after the onset, and has held since. This man (IV, 4) was a heavy smoker. He ceased using tobacco entirely and permanently within a month of the failure of sight, but his sight did not improve much, if at all, until about a year after failure and after ceasing to smoke. What share in the improvement, if any,

<sup>1</sup> Nettleship, "Bowman Lecture," loc. cit., p. 113.

<sup>2</sup> Ogilvie, *Trans. Ophthal. Sec.*, 1896, xvi, p. 3; Gould, *Ann. of Ophthal. and Otol.*, 1893, ii, p. 303, quoted by Nettleship, loc. cit.



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should be attributed to the abstinence from tobacco is an open question. Tardy recovery from what appears to be uncomplicated tobacco amblyopia is sufficiently well known.<sup>1</sup> Tardiness seems also to be a relatively common feature of recovery from Leber's disease, and it is possible that both factors are operative in some cases—a liability to Leber's disease that might have remained latent being brought out by tobacco, or possibly even by diabetes.<sup>2</sup> The unmarried woman (IV, 1), who died of diabetes at 39 is said by her brother (IV, 4) to have had bad sight during about the last year of her life, but whether the failure was due to Leber's disease or to retinitis, or even to cataract, cannot now be ascertained. Diabetes has been seen in two or three other cases of hereditary Leber's disease<sup>3</sup> and the occurrence of central amblyopia in diabetics who do not use tobacco has also now been established.

### DESCRIPTION OF THE PEDIGREE. (See figure.)

I, 1, A man, Smart; no information; age at death not known.

I, 2, Elizabeth Ayling, married to I, 1.

I, 3, sister of I, 2; married Boxall (not shown on diagram). It is not known whether I, 2 and 3, had any siblings.

These Aylings and Boxalls were from the Petworth or Lodsworth district of Sussex, and may be represented there at the present time.

I, 2, Elizabeth Ayling (Mrs. Smart) is known by several descendants to have been blind from about 30 years old till her death at the age of 80. She had an operation on account of her bad sight, presumably when about 30, but it did no good, and she lost what sight she had.

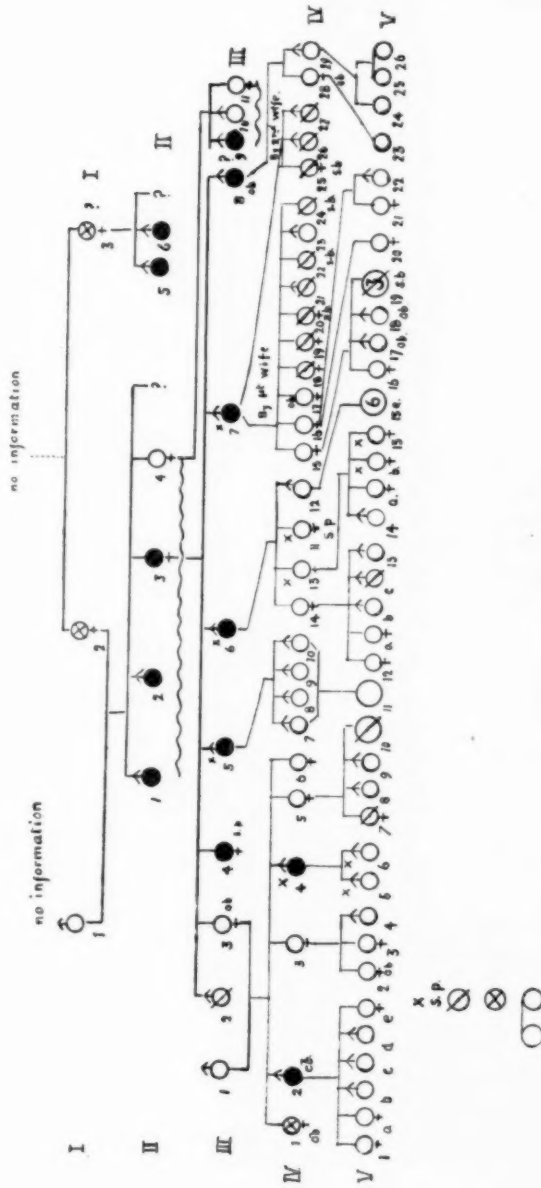
I, 3, her sister, Mrs. Boxall, is said by one relation (III, 6) to have had some kind of bad sight, but no one could confirm this. However this may be, it is practically certain from what III, 7, told one of us (E. Nettleship), on April 18, 1912, that her two sons (II, 5 and 6) had the family bad sight; we do not know whether they had any siblings.

II, 3, and her two brothers (II, 1 and 2) all became nearly blind between 25 and 30 years of age; from the description given by III, 6, in 1896, it is evident that the symptoms in his mother (II, 3) and at least one of her brothers were like his own, that their central sight was bad, but the periphery of the field relatively good. II, 1 and 2, died unmarried at 56 and 90 years old respectively. II, 4, had quite good sight and lived to be over 60; married a man named Lingfield and had the three children (III, 9, 10 and 11). One of these, the son (III, 9) is believed by his cousin (III, 7) to be affected, but his

<sup>1</sup> A. Hugh Thompson, "Tobacco Amblyopia: Some Cases in which the Interval between Cessation of Smoking and Improvement of Vision was unusually Long," *Roy. Lond. Ophthalm. Hosp. Reports*, 1896, xix, p. 406.

<sup>2</sup> Nettleship, *loc. cit.*, pp. 110 and 118.

<sup>3</sup> *Idem*, *loc. cit.*, pp. 117 and 118.



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place of residence has not been found (it may be Itchingfield) and there is no conclusive evidence. II, 3, who died at the age of 67, married a man with excellent sight (not shown on chart) and had seven children (III, 2-8), and so far as can be ascertained no miscarriages or stillbirths. We cannot find out whether II, 1-4, represent the whole issue of I, 1 and 2.

III, 2-8, seven children of II, 3. III, 2, died in early infancy. III, 3, good sight, died about fifteen years ago, aged 60, of a "fit"; seized suddenly and did not regain consciousness; had had two seizures before. Husband (III, 1), living (1912), aged 77, has good sight. They had two sons and four daughters, IV, 1-6 (see below).

III, 4, sight failed when she was 14 or 15 years old and was bad for some months, or a year, and then got quite well and remained so (testimony of III, 6, in 1896, and III, 7, in 1912, whose statements point to amblyopia, not mere accommodative failure); married many years, but no issue, died, aged 76 in March, 1912.

III, 5, James Luxford, Bedham, Pulborough. Seen with Dr. G. A. Spear, April 1, 1912, aged 75; found him at work on the road. A fairly intelligent man. Sight failed rather gradually when he was aged 17; for a time could not tell gold from silver and could not read at all; then improved a little so that he could read big letters with difficulty and tell gold from silver with care, but never regained power of reading ordinary print. Vision not tested, but he evidently has good peripheral sight; pupils small as in old age; no ophthalmoscopic examination. Had some advice in the early stage but has no hospital papers. Has had either four or five sons (not sure which), of whom youngest (IV, 10) died at the age of 10; other three living and see perfectly, and one at least is married and has some young children (V, 11) who are well and see well. III, 5, has had no daughters, and it is understood that the sons (IV, 7-10) represent his entire issue.

III, 6, George Luxford, 12, Kingsman Street, Woolwich, a timber workman; February, 1896, aged 56; E. Nettleship's patient at Moorfields Hospital. Vision rather better with right eye 18 or 20 J, very close, and less than  $\frac{6}{60}$ , not improved by glasses; well-marked absolute central scotoma from temporal side of fixing point inwards towards optic disk in each eye, periphery of F. full; pupils and tension normal; optic disks pale, especially on temporal side; arteries rather small in right, a few pale dots in Y. S. region in left. Sight failed "thirty years" ago—i.e., when he was aged about 25, perhaps younger. Seen again at his home by A. Hugh Thompson in 1912, aged 72, and found to be in same condition. Was very temperate when vision failed and only began to smoke about that time. Has three daughters and a son (IV, 11-14), of whom one (Mrs. Catheral, IV, 14) has to use glasses, but with them sees quite well; she (IV, 14) has had five children (V, 12, 12a, &c., to 13): V, 12, female, aged 21; 12a, female, aged 19; 12b, male, aged 15; 12c, male, died at 3½ months old; 13, male, aged 9; all the four living are reported to see quite well, but the boys have not yet reached the most susceptible age. Another daughter of III, 6 (IV, 13), Mrs. Berry, has four children (V, 14-15):

V, 14, male, aged 27, and 14a, female, aged 21, both reported normal; 14b, female, Ada Bessie, has been seen (September, 1912) by A. Hugh Thompson; she is aged 17, and has normal vision with each eye with +4.5D. spherical and +0.5D. cylindrical axis, vertical and normal fundus; V, 15, female, aged 15, also seen at same time and found normal in all respects.

III, 7, Job Luxford, 2, Marrowpit Hill, Edenbridge, formerly a wood "cleaver,"—i.e., maker of split oak rails for fences. Was at Moorfields Hospital from January to June, 1901, aged 58, under the care of Mr. Lang, and was told to stop smoking (had smoked  $\frac{1}{2}$  oz. a day). Full notes, including much that now appears in the pedigree, were taken by A. Hugh Thompson (*see* below). Vision began to fail when he was aged about 30 (say about 1873), but could see to sharpen his saw and even read till November, 1900, when vision rapidly got worse. When at Moorfields (January to June, 1901) could count fingers but not see J. 20 even with +3D.; refraction about Em.; central absolute scotoma about 15° diameter in each eye; optic disks atrophic, outer halves white; no nystagmus. Seen by E. Nettleship on April 18, 1912, aged 69, at his house; sight as in A. Hugh Thompson's notes and the disks moderately pale on Y.S. side. He says he cannot see the moon if he looks straight at her, but when he looks to one side "she comes into the sight." He is a healthy old man, now (April, 1912) aged 69; born December, 1842; fairly intelligent, and gives a clear account. Twice married—first when he and his wife were each aged 27; at second marriage he was aged 47 and his wife aged 31. By the first wife he had ten children (IV, 15-24), of whom only the first and second (IV, 15 and 16), females, and IV, 23, male, aged 32, single, are living (for the issue of IV, 15 and 16, *see* V, 16-22); third (IV, 17) died at 7 years of age; IV, 18, died at 6 weeks; IV, 19, died at 8 months; and the other four (IV, 20, 21, 22, 24) were stillborn or lived only a day. By the second wife, who was a widow when he married her—she being aged 31 and having been married six years to her first husband, but without issue—III, 7, had three children (IV, 25-27), of whom the first was stillborn, and the other two died aged 3 months and 2 months respectively.

III, 8, Albert Luxford, born nearly three years after III, 7, died suddenly at breakfast of "heart disease," aged 30 or 35; health had been failing for a time before. When in his teens, living at home and learning the "cleaving" work from his father, his sight got bad for a time, and the father (who had had the experience of the elder children, III, 4, 5, 6, 7, to judge by) thought the sight of III, 8, was going like the others, but after about a year it got quite well again. This account was given independently by III, 6, and III, 7, who were living at home at the time. III, 8, left two children, of whom the elder (IV, 28) died in her first confinement; the second (IV, 29) has three young children (V, 24-26), of whom 25 and 26 are twins. IV, 29, himself a bricklayer, is well known by his cousin (IV, 4) to have quite good sight.

IV, 1-6, issue of III, 3 (Mrs. Stenning); particulars from personal interview with IV, 4 (April 22, 1912): IV, 1, Emily Ellen Stenning, died, aged 39, of "sugar diabetes"; sight became bad a year or so before death, and she was

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quite blind the last day or two of life ; no medical details to be got. Was unmarried.

IV, 2, Percy Thomas, died of cancer of throat in Middlesex Hospital in 1907, aged 43 ; would be now 48 (1912) ; married and left six children (V, 1, 1a, &c.), viz. : V, 1, female, aged 21 (1912) ; 1a, female, aged 19 ; 1b, male, aged 17 ; 1c, male, aged 15 ; 1d, male, aged 13 ; 1e, female, aged 11—all reported to have perfect sight. The sight of IV, 2, failed at the age of 28, became worse than IV, 4, ever was, and did not improve ; went up from Dorking, where he lived, to Moorfields Hospital many times, but the letter is not forthcoming nor are there any notes of his eye condition at the Middlesex Hospital, where he died. He was a heavy smoker and drank too much.

IV, 3, Lucy Emma, Mrs. Phillips, aged 45 ; good sight ; three children, V, 2-4 (see below).

IV, 4, Frederick George, now aged 42 (April, 1912). When aged 28, in July, 1898, working as a baker, sight failed and got to worst in about two weeks ; was smoking  $\frac{1}{2}$  oz. black shag daily, and had been losing flesh owing to the nature of his work, as he thought. First symptom was failure to see the string of the decoy bird used in pigeon shooting, so that he could not tell whether he was aiming at the wild bird or the decoy. At his worst the moon was never quite blotted out to him, but he was unable to tell if she was full or not ; can now (April 1912) see her well and the stars too ; can now write fairly well and with +3D. reads words of about 6 J. [I (E. Nettleship) did not examine with ophthalmoscope.] Now is a small farmer, stout, ruddy and strong. Went to St. Thomas's Hospital under Mr. Lawford within a month of failure (August 4, 1898), and after attending as out-patient for six months was an in-patient from February 21 to April 18, 1899. Vision during all this period varied from  $\frac{2}{60}$  to  $\frac{6}{60}$  at many trials ; left being often a trifle better than right. There was a marked central colour scotoma, but, at first, no ophthalmoscopic change. About the middle of this time (November, 1898), and again in January, 1899, Mr. Lawford's notes record pallor of temporal half of each optic disk, nasal side good colour but edge blurred, no changes at macular region. Ceased smoking entirely after going to St. Thomas's Hospital in August, 1898. Whilst in the ward (February 21 to April 18, 1899) he was treated by constant current and for a month (February 27 to March 30) by subcutaneous injections of  $\frac{1}{30}$  gr. strychnine daily. These treatments had little, if any, perceptible effect on vision at the time. The following entries are taken from the ward notes : On October 11, 1898, right  $\frac{2}{60}$ , left  $\frac{3}{60}$ . February 21, 1899, admitted as in-patient ; right  $\frac{3}{60}$  and 20 J. at 4 in., scotoma for red and green as before ; left  $\frac{3}{60}$  and 19 J. at 4 in., scotoma as right. April 18, 1899, on leaving ward, right  $\frac{2}{60}$  and 18 J. at 6 in., left  $\frac{3}{60}$  and 14 J. at 4 in. *Much improvement, however, took place afterwards*, for on October 3, 1899, fully six months after cessation of treatment, he came up for inspection and had vision, right  $\frac{1}{18}$ , left  $\frac{6}{18}$  ; together  $\frac{9}{18}$  and 4 J. ; slight general contraction of each F. for white. IV, 4, has two children (see V, 5 and 6).

IV, 5, Kate Isabel, Mrs. Ayling, aged about 39, with good sight, has three children living (*see* V, 7-9). IV, 6, Laura, aged 36, unmarried, good sight.

The other members of IV and V have been referred to under their ascendants in III. There remain—V, 2-4, issue of IV, 3 (Phillips): V, 2, died, aged 5; V, 3 and 4, living, aged 9 and 5; V, 5 and 6, issue of IV, 4, aged respectively 7 and  $3\frac{1}{2}$  when seen (April, 1912); no miscarriages or stillbirths; V, 5, robust, healthy-looking and intelligent; V, 6, walks well and "talks like a lawyer," but is puny; was born at full term, mother having had no illness, but at birth weighed only  $4\frac{1}{2}$  lb. and was bottle-fed; mother's family history not inquired into. V, 7-10, issue of IV, 5: V, 7, died under twelve months; V, 8, aged about 14, and his younger brother (V, 9) *see* well; some others (V, 10) died in infancy or miscarried. V, 16-19, issue of IV, 15: V, 16, grown up and *sees* well; V, 17, died aged 6, and V, 18, aged between 2 and 3 years; V, 19, three stillbirths, unsexed. V, 20-22, issue of IV, 16: V, 20, born before marriage of IV, 16; V, 21 and 22, legitimate by a different man; all three *see* well; the youngest (V, 22) is aged 15.

#### DISCUSSION.

The PRESIDENT (Sir Anderson Crichtett, Bt., C.V.O.) said that members of the Section of Ophthalmology must feel very much indebted to Mr. Nettleship for the patience and assiduity with which he had devoted a good deal of his leisure to the following up of these hereditary cases. Personally he took a great deal of interest in them, because when he was a young man he remembered the doctrine of heredity was rampant, and many things were attributed to it which had not origin in that way. Then the pendulum swung in the opposite direction, and one was told that heredity was nonsense, and that seldom or never could it be traced. How such views could have been current was difficult to believe, because all must have recognized the likeness in family voices, and it was notorious that the lip of the Hapsburgs was carried from one generation to another. The Paulet family was another instance. He, his father, and Sir William Bowman had seen members of that family in whom there had been drooping of the eyelid, so that many unfortunate members of the family had to go through life with their heads so elevated that they wore an air of superciliousness which they did not deserve.

Mr. J. B. LAWFORD asked if there was obtainable evidence as to the relative malignancy of the condition in males and females. A large majority of the recorded cases occurred in males, and in them the number of partial recoveries was small; it would be of interest to know if the probability of recovery was greater or less in females.

Mr. A. HUGH THOMPSON desired to direct special attention to Case IV, 4, one of the cases which partially recovered after being a long time treated in St. Thomas's Hospital, he believed under Mr. Lawford. The suggestion was that in some of the cases which partially recovered, tobacco had some influence in the causation. In the full notes of the case given in the paper,

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it was mentioned that this man was a heavy smoker. When he entered St. Thomas's Hospital, naturally tobacco was stopped in the first place, and it had occurred to him to inquire, in cases of tobacco amblyopia in which recovery was very tardy, whether they might not have some connexion with Leber's disease. Sixteen years ago he collected some such cases, and published them in the Ophthalmic Hospital Reports; and it now occurred to him that they might possibly have been of this nature.<sup>1</sup>

Mr. NETTLESHIP, in reply, said he was not prepared to give on the spot a categorical answer to Mr. Lawford's question, but he thought in females this condition did not run a better course than in males. He would try to look up the point.

### Case of Retino-choroiditis Juxta-papillaris.

By A. W. ORMOND, F.R.C.S.

H. A. S., MALE, aged 20, was sent to consult me by Dr. Stewart, of High Barnet, on November 30, 1911. He had noticed some slight pain in his right eye a week previously (November 23), but it was not severe. On the Saturday (November 25) he found on waking up that he could see very little with this eye and he consulted Dr. Stewart, who sent him to me.

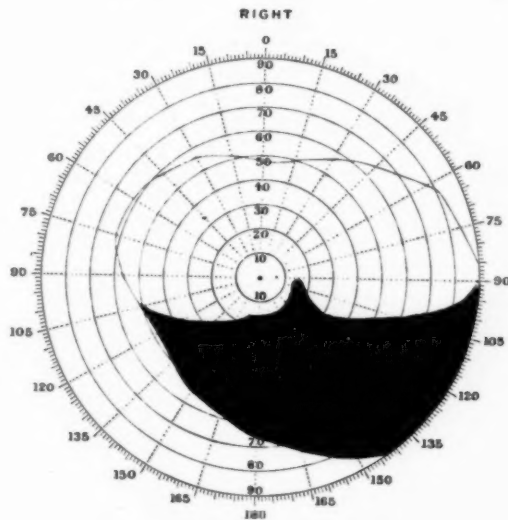
The patient is of an athletic build, tall, well proportioned, and plays football. He is very fair, with a well-marked "peach-blossom" complexion, long eyelashes, and rather thin, transparent skin. There is a history of acute and articular rheumatism in the family, but the patient has not suffered from either. He is slightly deaf, and has had a discharge from his left ear for some years.

On examination the right eye appeared to be quite healthy when seen from the front; the pupil was active, and no redness or congestion was visible. In the vitreous was a fine haze with opacities of various sizes, and one larger one coming forwards from below the nerve-head. The optic disk was hardly visible, the vessels could be seen radiating from a soft white mass, which covered the disk and a small area of the retina above. At first I thought the condition was due to a nerve change, and that I was dealing with a papillitis, the change being so circumscribed and located. On further examination, however, I found a small patch of keratitis punctata, and this led me to recognize that it really was a patch of acute choroiditis close to, but just above, the optic disk.

<sup>1</sup> See reference in footnote p. 10.



The field of vision was taken a week later, and it was found to have a very large area below, entirely absent. The macula was unaffected, but the blind area reached within  $15^\circ$  of the fixation point. At this time it was noticed that the arteries looked small and the veins full and purplish. The haze over the centre of the retina continued and the keratitis punctata was even more marked. Von Pirquet's reaction was definitely positive. I was uncertain whether the condition were due to tubercle or to a possible septic focus resulting from the ear trouble. My colleague, Mr. Mollison, examined his ear, and advised that the ossicles should be removed and the aditus enlarged by removing the outer wall. This was done and the discharge from the ear improved, although it did not for some months entirely disappear. On December 22, 1911, the vision of the eye was  $\frac{6}{36}$ . All the deposit on the posterior surface of the cornea had disappeared and the patient left the hospital.



H. A. S.—September 26, 1912.

The following note was made in January, 1912: At the macula are a number of large, white areas arranged in a star-shaped figure. The lower edge of the disk is just coming into view; the upper edge and beyond, over the base of the upper vessels is a dense haze, and through this some glistening white spots are seen.

Vision right eye  
 $\begin{aligned} &+0.5 \text{ spherical} \\ &-1.5 \text{ cylinder horizontal} \end{aligned} \quad \left. \vphantom{\begin{aligned} &+0.5 \text{ spherical} \\ &-1.5 \text{ cylinder horizontal} \end{aligned}} \right\} = \frac{6}{60}$   
 D—20

Vision left eye  
 $\begin{aligned} &-1 \text{ D. cylinder horizontal} = \frac{6}{60} \end{aligned}$

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February 14, 1912: The whole disk can now be seen. I have examined the patient on several occasions since, and the changes have always shown signs of improvement.

September 26, 1912: The eye was examined again to-day. The whole disk has an oval shape with a fan-shaped white area above. The margins of the disk are surrounded by a soft, white haze, and the centre is still covered by some filmy exudation, which can be seen coming forward into the vitreous. There are several streaks of exudation over the vessels, and all are attached to the retina. The superior retinal arteries all show some alteration. Those going directly upwards and inwards are reduced to fine, almost invisible, threads, and the superior temporal ones are like "gold wire" in appearance. The fan-shaped mass above the disk is obviously subsiding into a patch of choroido-retinal change, although the amount of pigment to be seen at present is *nil*, but the pale yellow colour and sinuous outline of such patches is well seen. The absence of pigment may be associated with the general fairness of the patient. The field of vision remains unchanged. Vision as before.

Under the title "*Retino-choroiditis Juxta-papillaris*," Professor Jensen, of Copenhagen, published four cases in Graefe's *Archives*, which are, undoubtedly, clinically the same as this one.<sup>1</sup> They were all young people, aged 20, 23, 34, 44. The macula escaped in all, and the central vision ultimately was good. The subjects were healthy and free from any taint of syphilis or gonorrhœa, but were not specially examined for tubercle. Three had vitreous opacities and soft white œdematous patches of acute choroidal change, touching the optic disk. The blind sector in each case included the blind spot, reaching to it and radiating from it to the periphery, and in the affected area all perception of light was lost. The other eye was normal, and the changes in the affected eye were confined to the single area in the disk. When the inflammation subsided a mottled patch of superficial retino-choroidal change remained. The vessels of the affected areas showed smaller and narrower than the remaining ones. There is no doubt that the case of H. A. S. is in every way similar to Jensen's cases, and I think throws some light on those patches of choroido-retinal change lining the optic disk, which we sometimes see when making an ophthalmoscopic examination.<sup>2</sup> Mr. Brewerton, in reviewing Jensen's article, made the suggestion that such cases were probably tuberculous in nature.

<sup>1</sup> *Arch. f. Ophthalm.*, Leipz., 1909, lxix, pp. 41-48.

<sup>2</sup> *Ophthalm. Review*, 1908, xxvii, p. 319.

I certainly think my case was, although it was complicated by the possibility of its being due to a septic process derived from the ear of the opposite side. The patient did, however, exhibit definite signs of tubercle, and the probabilities are in favour of this being the ætiological factor.

The defective area in the field of vision is clearly due to the obliteration of a branch of the central retinal artery by the pressure of the inflammatory swelling.

### **Case of Pemphigus of the Conjunctiva followed by Essential Shrinkage of that Membrane.**

By A. W. ORMOND, F.R.C.S.

W. H. W., AGED 24, male, was in Guy's Hospital seven years ago with bullæ of the conjunctiva. The conjunctiva then was much shrunken, the condition having first started when patient was aged about 11. He was able to read until he was aged 17. He is not suffering any pain now.

Present condition: Vision of right eye, hand movements at 1 ft.; vision of left eye,  $\frac{1}{60}$ . The symblepharon is well marked; patient experiences an unpleasant sensation of pulling when he moves his eyes. No bullæ can be seen now and the acute stages have passed away. The conjunctiva is thickened and completely covers the right cornea, and almost the whole of the left. He does not complain of much, beyond some sensation of unpleasantness in extremes of heat or cold or severe wind; the condition is slowly getting worse.

#### **DISCUSSION.**

Mr. ORMOND said that his object in bringing the case was to ask advice as to treatment. It was very distressing, and the patient was only aged 24. He saw him seven years ago, and he got tired of treatment by arsenic. He had not seen him from that time until the present, and the sight was now so bad that if possible something should be done. He proposed to remove as much of the growth from over the conjunctiva as he could, clearing it as far back as possible, and put mucous membrane from elsewhere in its place.

The PRESIDENT said they must acknowledge that this was the kind of case which humbled them, because so little that could be done brought benefit. Perhaps what Mr. Ormond suggested offered the only chance.

Mr. HERBERT FISHER said he had had under observation a case of pemphigus of the conjunctiva, in which the patient developed vesicles on the mucous membranes and skin. It seemed reasonable not to attempt surgical treatment, but to try to check the progress of the disease, for in one eye the condition was hopeless, while in the other the cornea was only beginning to be involved. A vaccine was accordingly given which had been made from cultivations from the vesicles, but it was not persisted in for long. Mr. Lawford had some further knowledge of that case, as he saw it later, and perhaps he would mention it.

Mr. J. B. LAWFORD said he saw the patient to whom Mr. Fisher referred, and watched him over a period of three months. The vaccine treatment was continued during the greater part of that time, the vaccine being made, as Mr. Fisher said, from the patient's vesicles. It was very difficult to say whether the treatment did any good. His own opinion was that it retarded the progress of the disease; the patient did not get worse while he was under observation. He lived in Australia, and had to return to his home, and Mr. Lawford had not heard of him since. It was difficult to say anything about such treatment on the experience of only one case, but, on the whole, his impression was that it was worth trying.

Mr. BISHOP HARMAN said he had recently had a case of the kind under observation for three years, in an old gentleman who had pemphigus very badly in his larynx, pharynx, mouth, and both eyes. Happily he died before he became quite blind. Everything possible was done by a famous laryngologist and a skilled skin physician; both vaccines and arsenic were tried, but no medication stayed the progress of the disease. To check the entropion he did a small skin and muscle operation, turning out the lid, and that comforted him for a time. Then he trained the patient's wife to pull the eyelashes out systematically, and that gave him some comfort; further relief was obtained by wearing narrow strips of strapping to lift the drawn-down upper lids. The temporary alleviation of symptoms was all that they could expect with their present knowledge.

Mr. ORMOND, in reply, said that seven years ago there were vesicles, but they had disappeared. At that time he removed a small piece, and had it injected into a guinea-pig, to ascertain whether there was any tuberculous basis, but found there was not.

### Drawing of Semilunar Retinal Hæmorrhages (so-called Subhyaloid Hæmorrhages).

By J. HERBERT FISHER, F.R.C.S.

THE patient, from whom the drawing exhibited was taken, was H. B., male, aged 45, seen at Moorfields Hospital on October 22, 1912. When washing himself in his scullery—and probably in a stooping posture—hearing his children quarrelling on the stairs, he hurried along the passage in a passion to quell the disturbance, and on returning to the scullery found his sight blurred. It appeared as if he saw through a red film with his left eye. This occurred eight days before his visit to the hospital. The right eye was normal in all respects. The vision of the left eye was  $\frac{6}{18}$ .

Ophthalmoscopic examination revealed considerable hæmorrhagic opacity in the vitreous humour. On the upper nasal vein was a dense extravasation of blood at a considerable distance beyond the disk margin. From the peripheral limit of this hæmorrhage depended a thin streak of blood leading to a typical D-shaped hæmorrhage situated beyond the outer margin of the optic disk. The dependent streak was very faint at its upper part, but became wider and more conspicuous as it merged into the subhyaloid hæmorrhage. At its upper end it only partly obscured some faint retinal vessels; whether they passed behind or in front of it cannot be determined. The second smaller, but quite characteristic, D-shaped hæmorrhage lay adjacent to the lower edge of the optic disk, rather towards its outer side, and blood in association with this was found on the lower part of the disk surface. Three distended veins and one descending artery were in relation to this second subhyaloid hæmorrhage, and hidden by it. The blood probably came from the innermost of these three large veins.

The blood floating in the vitreous evidently explained the red film which struck the patient at the outset of his trouble, so that blood obviously found its way into the vitreous very promptly. At the time of his visit a vitreous haze concealed the proximal part of the upper nasal vein completely from view.

The drawing exhibited (*see Plate*) was made on October 24. By this date the subhyaloid extravasations were already smaller and the veins less turgid. The faint dependent streak was noticed also to extend in

## 22 Fisher: *Drawing of Semilunar Retinal Hæmorrhages*

a long arc in the retina above the optic disk. This extension was not noticed at his first visit, and I believe was not present, though it may possibly have been obscured by the vitreous haze. The blood-vessels are not degenerate. The urine is normal. I believe that venous obstruction—not very complete—occurred in the central vein in the head of the nerve.

November 1, 1912: The changes in the fundus and vitreous are steadily improving.

The case is of interest, as it appears to me conclusively to prove the venous origin of these peculiar hæmorrhages. It shows that blood so extravasated may find its way with great rapidity into the vitreous humour. It does not help greatly to decide the situation of the D-shaped hæmorrhages; this point, however, appears to have been settled by the pathological examination of the case, which I reported in the *Royal London Ophthalmic Hospital Reports*, vol. xiv, 1896. The blood is primarily poured out beneath the internal limiting membrane of the retina, through which, however, it finds little difficulty in passing to form a film immediately overlying the retina. Whether in this situation it lies between the internal limiting membrane and the hyaloid membrane, or whether, indeed, a true hyaloid membrane exists at all, are points upon which differences of opinion remain.

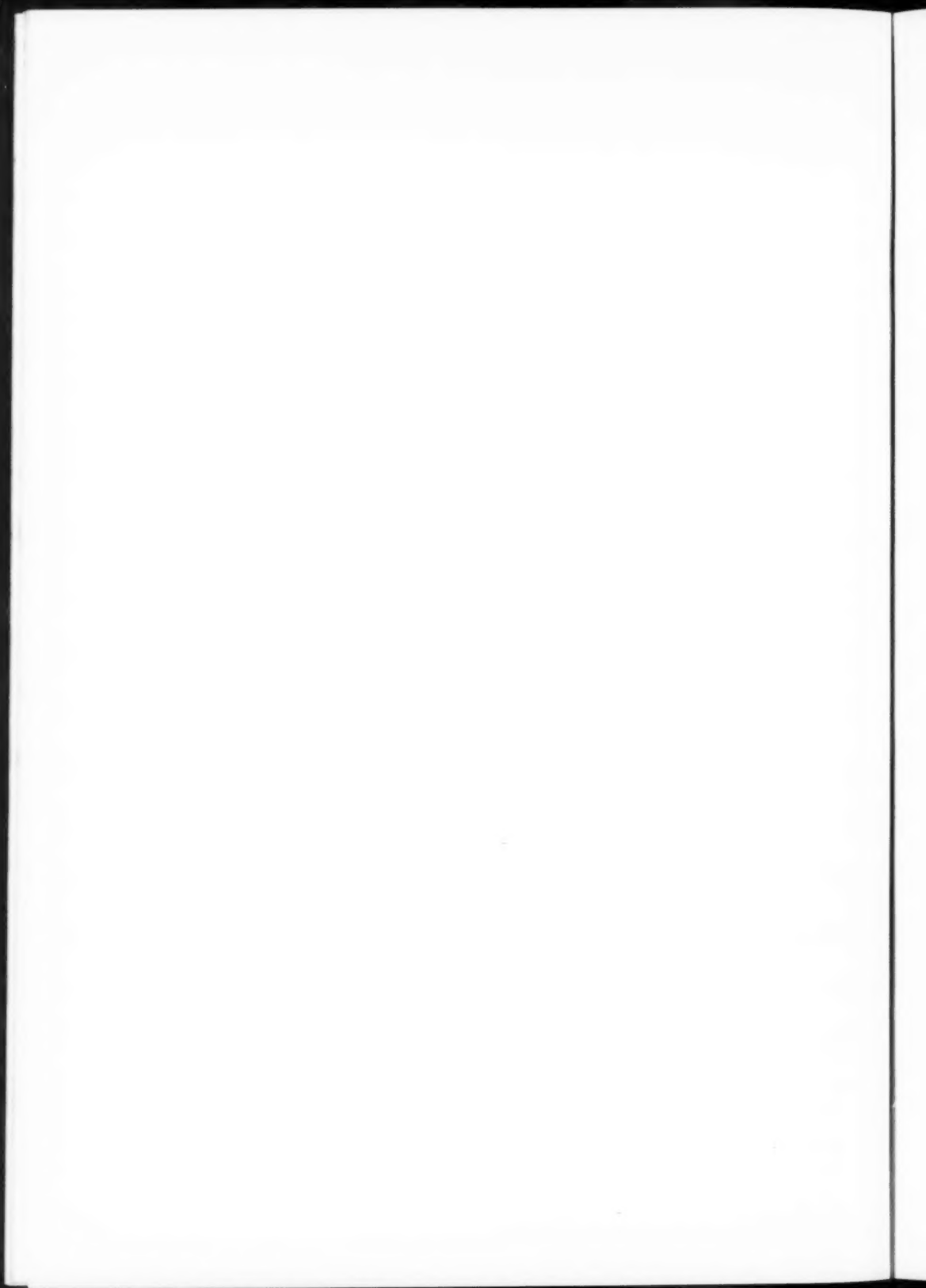
Since I reported the first case of pathological examination in 1896, further examinations of these hæmorrhages have been several times reported. In few of them have the typical D-shaped hæmorrhages been identified during life with the ophthalmoscope, and subsequently identified in the microscopic section. In some of those reported, the hæmorrhage was obviously not of the characteristic kind at all. Benedek has collected in literature eleven examinations. In only one of these was blood found in front of the internal limiting membrane. Harms has reported two cases, one of which was seen with the ophthalmoscope, and in this case the blood was lying in front of the internal limiting membrane.

We are in the habit of preserving in ophthalmology terms hallowed by custom, even though they are not pathologically accurate—e.g., phlyctenule, keratitis punctata, &c. When, however, a term such as subhyaloid hæmorrhage is really misleading, I think the time has come to discard it; this term does not date back to pre-ophthalmoscopic days, and I venture to suggest that "semilunar retinal hæmorrhage" be substituted for it. Such a term, or its translated equivalent, would be available in all languages.



*FISHER: Semilunar Retinal Hæmorrhages (so-called subhyaloid hæmorrhages).*





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## DISCUSSION.

The PRESIDENT asked whether there was any increased arterial tension in this case. He considered Mr. Fisher's suggestion as to the term to employ a very sensible one, and it would be well if the old name could be got rid of, just as was done in the case of the term, "choked disk," at the instigation of Sir Jonathan Hutchinson.

Mr. FISHER, in reply, stated that there was no obvious increased arterial tension. The patient was a man aged only 45, and had healthy vessels.

### Case of Partial Oculomotor Paralysis, with Synchronous Clonic Contractions of Muscles supplied by the Third Cranial Nerve.

By R. A. GREEVES, F.R.C.S.

A HEALTHY girl, aged 8; eight other children, all healthy. Drooping of the left eyelid noticed since an attack of measles a year ago; till then the left eye appeared the same as the right. The left eye does not close fully during sleep. Right eye: Vision  $\frac{6}{6}$ , pupil reactions normal, consensual light reaction present. Left eye: Vision  $\frac{6}{60}$ , with +2D. =  $\frac{6}{24}$ . Partial ptosis. The eye cannot be moved inwards beyond the middle line; upward and downward movements absent; outward movement good; slight downward and outward movement preserved.

The following series of movements occur rhythmically and synchronously: (1) The drooping lid is raised, after a few preliminary tremulous movements; (2) the eye is moved inwards to the middle line; (3) the pupil contracts fully; (4) a spasm of the ciliary muscle occurs, the refraction of the eye becoming about 3.5 dioptries more myopic. The lid then drops, the eye moves out, the pupil dilates, and accommodation is relaxed. The cycle of movements is then repeated. This cycle has been timed on several occasions, and the time has been found to vary on each occasion. But the contraction stage of the cycle has always been found to last exactly as long as

the time taken by the rest of the cycle—for instance, on one occasion the pupil remained contracted for twenty seconds, and took twenty seconds to dilate and contract again, there being no appreciable stage of dilatation, and the whole cycle lasting forty seconds. On some occasions the cycle has occupied a longer and, on others, a shorter time than this. The pupil does not react to light. The left eye is independent of the right, except in that the consensual reflex in the right eye is present, and that concomitant movements are, as far as possible, preserved. Light, and attempts at accommodation, do not affect the movements.

Axenfeld and Schürenberg described a case in 1901, and quoted three others previously reported. They pointed out that these cases presented the same clinical picture. Two had been described by Rampoldi in 1884, and one by Fuchs in 1893. Since then six have been described. In each there was incomplete ptosis, with a degree of paralysis of the muscles supplied by the third nerve, and in all, when it was possible to determine the point, a contraction of the ciliary muscle accompanied constriction of the pupil. One case exactly resembled the present one; in three the lid was raised without adduction of the eye, and in one there was adduction without lid movement. In one case the pupil reacted to light, and in two an attempt at adduction caused lengthening of the period of contraction. In six cases there was no lid movement at all.

The effect of drugs has been investigated. Atropine and eserine cause permanent dilatation and contraction respectively, cocaine widens the mydriasis and diminishes the constriction of the pupil, but has no effect on the movements. Other observers have noted similar results. In one case the movements were observed to go on during sleep. The time taken by the cycle has varied in each case.

Though some of the cases were adults, there has always been a history of ptosis and squint in early infancy. In Fuchs's case there was a history of the condition having followed an inflammatory affection of the throat in the second year. Axenfeld and Schürenberg<sup>1</sup> came to the conclusion that the condition was a congenital one. Franke,<sup>2</sup> who wrote on the subject in 1909, came to the same decision; he reported two cases. One of these was aged 16, and he found that he had seen her previously when she was 6 months old, and had noted

<sup>1</sup> Axenfeld and Schürenberg, "Klin. Monatsbl. f. Augenheilk.", 1901, xxxix, pp. 64-73.

<sup>2</sup> Franke, *Klin. Monatsbl. f. Augenheilk.*, 1909, xlvii, part ii, p. 582.

the ptosis, but not the other symptoms. He thinks the age of the patient may have been the reason for his missing them. The age in the present case—i.e., 7 years—is very much the latest at which the condition has been noticed first.

All the cases but one have been in females. In one case both eyes were affected. Fuchs pointed out that the lesion must be a nuclear one. Axenfeld and Schürenberg thought the condition resembled athetosis. Bielschowsky suggested rhythmical vasomotor changes in a previously damaged nucleus. Cramer<sup>1</sup> described a case of congenital rhythmic contractions of both pupils, but in his case there was no paralysis, and the light and accommodation reflexes were normal.

#### DISCUSSION.

The PRESIDENT said the Section was much indebted to Mr. Greeves for bringing forward this exceptionally interesting case. He had not himself seen one quite similar. The interest was added to by the fact that now they were able to show that it was not congenital, and therefore this case, although that of a quite young patient, would probably become historic.

Mr. BISHOP HARMAN asked whether Mr. Greeves had any idea why there should be what appeared to be a kind of alternation in the phenomena between the two eyes. He (Mr. Harman) threw out the suggestion that there had been in this case something like anterior poliomyelitis of the left third nerve nucleus, and consequent loss of innervation of the corresponding set of muscles. There were known to be some crossed fibres from the corresponding nucleus of the other side of the brain, and he asked whether it was possible that after a period of comparative inaction of the healthy nucleus, some impulse got across to the cut-off muscles, and produced these rhythmic contraction phenomena. By way of testing this, he tried to see whether in this patient there was a phenomenon which he had exhibited in a patient shown at the Ophthalmological Society several years ago; that patient was a man who suffered from monocular ptosis following nuclear gumma. Movement of the paralysed lid produced a veritable see-saw. If one lifted the drooped eyelid the upper lid of the other eye dropped down, and when the ptosis lid was released the upper lid of the other eye was lifted up. Once or twice he thought this see-saw phenomenon could be obtained in this present child. If that phenomenon could be established in the present case, it would be fair evidence that there was some active innervation coming from the healthy side to the unhealthy.

Mr. NETTLESHIP asked Mr. Harman if the ptosis was complete on the one side. He thought it was probable that the effort to raise the lid consensually raised the other too much; and when the effort ceased, it dropped to the normal extent. That seemed to be the explanation of some such cases.

<sup>1</sup> Cramer, *Klin. Monatsbl. f. Augenheilk.*, 1911, xlix, part i, p. 201.

## 26 Parsons: "*Mooren's*" Ulcer with Ulceration of Sclerotic

Mr. HERBERT said that last year he had had a similar case in a youth, the right eye being affected, the left eye normal. The rhythmic opening and closing of the eye had been noticed since the age of 3 months, without marked change. As Mr. Herbert had not the notes of this case at hand, they would probably be published shortly.

Mr. GREEVES, in reply, said that he could not make out a relationship between the movements of the two eyelids. He thought the right pupil was a little unsteady, but this seemed to have nothing to do with the contractions and dilatations of the other pupil.

### "Mooren's" Ulcer associated with Ulceration of the Sclerotic.

By J. HERBERT PARSONS, F.R.C.S.

F. D., AGED 49 years 8 months; married twenty-seven years, one child, only lived five months, no miscarriages. Eyes said to have been bad at birth and for six months afterwards. Eighteen years ago she had a "corneal ulcer" on the left eye, and a few months later a similar "ulcer" appeared in the right eye. For five years on and off both eyes were bad and then for six years there was a period of quiescence. Seven years ago she attended Moorfields Hospital as an out-patient, and at that time there was a fairly dense corneal opacity in the left eye, extending right round the cornea above to the limbus, a small portion only of the cornea at the centre being clear. One or two small nodules were present in the sclera on the outer side close to the limbus. Vision in left eye at this time reduced to counting figures at 1 ft. Nothing abnormal seen in either fundus. Cornea slightly anæsthetic. The "nodules" in the sclera broke down, leaving shallow ulcers with much vascularization in their vicinity. They proved very obstinate to all kinds of treatment, such as dusting with calomel, painting with protargol, the galvano-cautery, and even peritomy. She continued under treatment some three years, and finally the "ulcers" healed. There was considerable doubt as to the nature of the affection at this time. At first it was thought the scleral nodules might be of the nature of a neoplasm, and finally the diagnosis of scleral gumma was made.

Both eyes now remained quiet for a period of a little over four years, when she again came up for treatment, this time the right eye being affected in a similar way to the left four years previously. When

she came under observation in August of this year the appearance presented by the right eye was somewhat that of a localized episcleritis, the patch being close to the limbus on the outer side. The left eye was quiet and has remained so throughout the present attack. Vision in right  $\frac{6}{18}$ , left counts fingers. The "episcleritic" patch soon broke down, leaving a shallow, circular, clean-cut ulcer close to the limbus on the outer side. Some ulceration next appeared on the contiguous portion of the cornea and spread rapidly in a circumferential direction. At one time it was very deep, almost down to Descemet's membrane, but never actually perforated, the pupil always dilating with atropine. At first both ulcers were very obstinate to treatment, but during the last two weeks or so have shown signs of healing. Posteriorly to the scleral ulcer, however, a large nodule has appeared in the sclera, and is surrounded by an area of intense vascularization.

Upon admission the patient was suffering from bad pyorrhœa alveolaris and a superficial suppurative condition of the pinna of the left ear, both of which have slowly responded to treatment, and are now almost well. A general examination of the patient has failed to throw any light on the case, as have also attempts to obtain cultures from the scleral ulcer. Wassermann's reaction is negative, and the urine is normal. Tuberculin reactions have not been tried.

The local treatment which has been tried for the scleral ulcer upon this occasion includes painting with  $\text{AgNO}_3$  (10 gr. ad. 1 oz.), pure carbolic acid, powdered calomel and iodoform, zinc ionization, and, finally, the galvano-cautery, which seems to have done more good than any of the others. A course of general antispecific treatment has also been given.

The corneal condition is characteristic of Mooren's or chronic serpiginous (Nettleship) ulcer of the cornea. I have been unable to find any record of such cases associated with ulceration of the sclerotic.

#### DISCUSSION.

The PRESIDENT said that when Mr. Parsons called his attention to the case his first impulse was to suggest that it was a case where surgical and mechanical rest might afford the best chance. The point was as to how that was to be secured. He had suggested it would be well to stitch the lids together, but he was reminded that it was the poor woman's only eye. He therefore advised cauterization and careful packing of the orbit, for a time, at all events. But it was not a promising case.

Mr. HOLMES SPICER said it was difficult to make out the relationship of the various diseased parts. The patch on the sclerotic seemed independent of the ulcer; and if the sclerotic lesion was of the same nature as the corneal one, there were two Mooren's ulcers. It looked like a patch of necrosed sclerotic. He had seen a Mooren's ulcer in which the conjunctiva was involved; there was the ulcer on the cornea, but it extended some distance over the margin of the limbus, and was deeper in the sclerotic than in the cornea. With regard to suture of the lids, in a very bad case of Mooren's ulcer which he had treated, the lids were closed together a long time, but it had no effect on the ulcer.

Mr. NETTLESHIP said the name "Mooren's ulcer" was applied because Mooren first described it carefully. The term "ulcus rodens" had led people to think it was rodent ulcer, and it had more than once been called malignant ulcer.<sup>1</sup>

### Case showing a Modification of Herbert's Flap Operation for Chronic Glaucoma.

By LESLIE PATON, F.R.C.S.

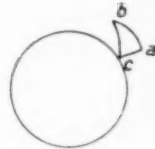
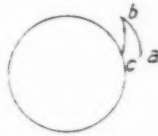
THE most important points in favour of Herbert's operation are the simplicity of its technique and the small amount of risk to the eye involved. The most serious disadvantage, in my hands at least, has been that the drainage established has not always been permanent, and in some cases the leakage has ceased within a very short time. In the present patient the operation was modified so as to obviate that difficulty.

*Mode of Operation.*—The conjunctival incision is made 5 to 6 mm. from the limbus and the conjunctiva lifted towards the cornea. The narrow keratome is inserted about 3 mm. from corneal margin, being held between a radial and tangential position, but nearer tangential. After the keratome incision is completed, the blunt-pointed Langs needle-knife is inserted, carried to one end of the incision, and then a cut is made obliquely forward towards the corneal margin, so that it finishes very nearly opposite the other end of the keratome incision. A small radial cut is then made from point *a* towards point *c*. These three cuts map out a triangular flap held only by one tiny point of attachment at *c*. If this is cut through the same effect is produced as

<sup>1</sup> Note.—I myself proposed the term "Mooren's ulcer" as a substitute for "ulcus rodens" in 1902; see *Trans. Ophthal. Soc.*, 1902, xxii, p. 103, where the reason for the proposal is explained.—E. N.



in simple trephining. The aim, however, of the operation is not to cut through this, but to leave the flap attached and (a) either ease it out under the conjunctiva as in the right eye of present patient, or (b) turn it into the anterior chamber as in the left eye.



Flap turned out and lying under conjunctiva.



Flap turned in and lying in anterior chamber.

#### DISCUSSION.

The PRESIDENT said the modification of the operation which Mr. Paton had made was a very interesting one, but Mr. Paton himself would say it was only on its trial. He hoped that, later, Mr. Paton would give the results of a longer experience. He asked if there was any object in going through the conjunctiva as well as the sclerotic in Mr. Herbert's operation.

Mr. HERBERT said that, in Mr. Paton's modification, two changes were made from the ordinary small-flap sclerotomy. There was the reduction of nutrition of the flap by narrowing its base greatly, and there was the displacement of the flap. In a number of cases in which it had seemed likely that the ordinary operation might fail, he had attained the first of the above two objects by a very easy modification. The operation was performed with modified Bishop Harman's twin-scissors.<sup>1</sup> The scissors were lighter and narrower than the original, the male blade being only 1.5 mm. broad, and they were angled so as to be applicable at the upper margin of the cornea. After making the usual 3.5 mm. keratome incision subconjunctively (fig. 1, b), one added two scissor cuts in the ordinary way, but with the scissors pressed to one end of the small section. The conjunctiva was cut with the scissors

<sup>1</sup> Suggested by Mr. Laws, and made by Wilhelm Walb, Nachfolger, Heidelberg.

together with the sclera, no conjunctival flap being reflected. Then the scissors were simply moved over towards the other end of the keratome incision, and two fresh cuts made in the positions shown by the dotted lines in fig. 2. Thus three very narrow flaps were made (fig. 3). The lateral flaps interposed a barrier to the penetration of new blood-vessels from the sides into the central flap, which remained consequently imperfectly nourished. The union of the two central cuts was imperfect, and increased filtration was thus obtained; but this applied rather to the final result than to the immediate result. There had been transient rises of tension seen in some of the cases (secondary glaucomas) operated upon. An objection to the operation was the need of guarding especially against adhesion of iris to the numerous incisions and against prolapse, which would be serious in that it would be uncovered by conjunctiva. Thus the addition of an iridectomy was frequently indicated, particularly in eyes with very shallow anterior chamber, and this added somewhat to the severity of the operation. Otherwise he thought it was good. He had also performed this triple-flap sclerotomy under a reflected conjunctival flap in three cases without iridectomy. In two the result had been unsatis-



FIG. 1.



FIG. 2.



FIG. 3.

*a* = site of keratome puncture in conjunctiva. Subsequent incisions in conjunctiva omitted for the sake of clearness. (N.B.—The primary scleral puncture is rather far from the corneal margin.)

factory—in one of the two disastrous. A complication had followed which he had never seen in any other "small flap" operations. The iris had adhered to the incisions, completely blocking filtration through them. The tension had risen and the flaps had bulged forward so much that the ciliary body was exposed under the conjunctiva beyond the scleral flaps. In one of the cases the protruding ciliary body was not even covered fully by conjunctiva. This case went slowly to the bad, apparently through infective trouble. In both cases the bulging of the flaps and the tension of the eye were reduced by a second operation about a week after the first. But in the one eye cataract slowly formed (possibly, though not certainly, due to injury at the second operation), the field of projection of light became considerably contracted, and five months later there was iritis for a week or two. In both of these eyes the anterior chamber was exceptionally shallow before operation. Though the above complication might have been prevented by iridectomy, Mr. Herbert preferred also, as an additional precaution, to cut through the conjunctiva with the scissors to ensure early free leakage.

## Section of Ophthalmology.

December 4, 1912.

Sir ANDERSON CRITCHETT, Bt., C.V.O., President of the Section,  
in the Chair.

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### Discussion on the Physiology of the Intra-ocular Pressure.

Opened by LEONARD HILL, M.B., F.R.S., and  
E. H. STARLING, M.D., F.R.S.

DR. LEONARD HILL, F.R.S.: I feel, and I think Dr. Flack agrees with me, as if we are rather intruding here in venturing upon a task such as this. It seems almost an impertinence for physiologists to enter upon a subject which is so familiar to all you experts in ophthalmology. But some researches which we have been carrying out on the relation of the circulation to secretion led us to investigate the eye, and the results of our investigation have been published recently in the *Proceedings of the Royal Society*; <sup>1</sup> these we propose to bring before you to-night. The first task we set before us was to try and measure the intra-ocular pressure. That has been done by many observers before. Mr. Thomson Henderson and I made preliminary experiments. We were not satisfied with using the ordinary hypodermic needle, for we could not avoid leakage, or at all events it is very difficult indeed to avoid leakage, in the track of such a needle. That led to my devising a special needle, a sketch of which I show you on the screen (fig. 1). Dr. Flack and I have employed this in our measurements of the intra-ocular pressure. It is made of two tubes, an inner and an outer. The inner tube can be rotated by means of a handle, and there is an eyehole in it which corresponds, in a certain position of rotation, to an eyehole

<sup>1</sup> *Proc. Roy. Soc., Ser. B*, 1912, lxxv, p. 459.

in the outer tube. When the two holes are opposite the aqueous humour can pass into the inner tube. If we rotate the handle right round, the eyehole of the inner tube is no longer in correspondence with the eyehole in the outer needle, and the needle is closed. As we put it in closed, no aqueous can escape. We have a conical shaped needle, and it goes in as a cone, and that prevents leakage, and when it is in, we rotate the needle, until the eyeholes correspond, and so the pressure of the aqueous can be measured. The aqueous pressure is measured by the compensatory method (fig. 2) which I employed for measuring the pressure in the brain. The inner tube of the needle is connected with a length of glass tubing of fine-bore which in its turn is connected by a piece of rubber tube with a pressure bottle and a mercury manometer, or a water manometer, if you like, it does not matter which. An air bubble is introduced into the glass tube, and the position of it marked when the pressure is at zero, that is to say, at atmospheric pressure. The zero position is

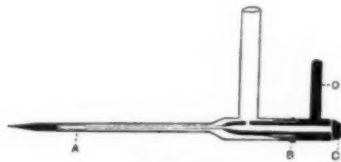


FIG. 1.

A marks the position of the eyeholes in the inner and outer tube which correspond when the handle D is in the position shown. B, cork. C, screw, which can be removed when cleaning the inner needle.

obtained when the eyehole is open in the needle, and the pressure bottle is lowered to such a point that the water within it is at the same level as the eyehole, and ceases to flow out. Having marked the position of the air bubble on the glass tube, we push the closed needle into the aqueous, and transfix the anterior chamber with it so that it is steady. We support the needle so that it exerts the least possible tension on the eyeball, and then rotate the handle so as to open the needle. The air bubble is pushed out, and the moment it is so pushed we bring it back to the zero mark, by raising the pressure bottle, and thus compensate the pressure of the aqueous without letting any of this fluid escape. Then we read the pressure. When inserting the needle try to get as near the edge of the cornea as possible, and push it right through.

The hole lies in the aqueous, and we make sure it is free in the aqueous, and we can see it in there. It is very important to support the needle, because any tension on the eyeball will raise the pressure of the aqueous, and that is a great source of error. Mr. Thomson Henderson has suggested another source of error—namely, that the introduction of such a needle into the eyeball may cause some reaction in the eye; a temporary obstruction of the circulation occurs during the introduction of the needle, and a subsequent dilatation of blood-vessels probably results, which raises the pressure to a greater level than the normal. Such a reaction would soon subside. We have controlled the reading of the needle in this way. We pushed into the same eye or into the opposite eye a hypodermic needle, a very small

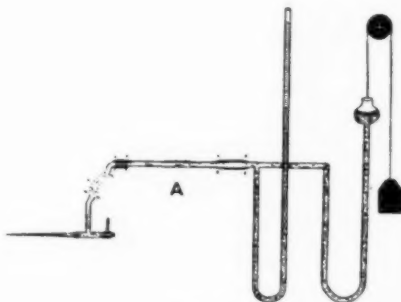


FIG. 2.

Compensatory method of measuring intra-ocular pressure. The glass tube A contains an air bubble.

one, connected with a gauge which I use for measuring blood-pressure. The gauge is a glass tube, open at one end and closed at the other. At the closed end, by which it is held, there is a piece of solid glass. The lumen is of fine bore, and ends in a tiny air reservoir. The open end is put into potash solution, and a meniscus of this fluid rises to a side hole which is placed near the open end. A rubber tube is then slipped over the open end so as to cover the side hole. This rubber tube is connected with the hypodermic needle. The gauge forms a spring manometer; the air is the spring. It is calibrated in millimetres of mercury, from 0 to 100. When the needle is pushed into the eye through the cornea, the aqueous drives up the potash meniscus from the zero point (the level of the side hole), and then we

read the pressure. We do it the moment after the needle goes in, because the aqueous may escape quickly round the track of such a needle. The readings taken by means of this gauge are not different from those obtained with the larger needle. The result shows that the aqueous pressure varies within fairly wide limits, depending upon the blood-pressure. The higher the arterial pressure, the higher is the aqueous pressure. We have got readings as low as 16 mm. Hg. in one cat under chloroform and with a low arterial pressure, going up under ether or urethane narcosis, when the animals were in good condition, as high as 62 mm. Hg. Variations of that kind, agreeing between arterial and aqueous pressure, left no doubt in our minds on the point. In comparing the readings with the hypodermic needle with those with our needle, done by the compensation method, we got readings which seemed to agree. So we could not find any source of error.

So much for the aqueous pressure. We do not very much mind what the aqueous pressure is, as it is not of very great importance except that it is positive; 30 to 40 mm. Hg. was commonly obtained in cats. It is very important that it should be positive, and considerably positive, because that keeps the eyeball as a perfect optical instrument. The eyeball is distended, in our opinion, by a secretory pressure, and that keeps it as a perfect optical instrument, perfect in its shape, equally distended all over. And to preserve that a positive pressure is required, and it does not seem to matter very much whether that positive pressure varies from 10 mm. Hg. to 50 mm., for the outer coat of the eyeball is firm enough to resist any distension, and the eyeball remains the same shape and size under very different strains. When a man is making an effort he may have an arterial pressure of 150 to 200 mm. Hg. The pressure of his aqueous may then be 50 mm. Hg. When he is at rest his arterial pressure will be about 100 mm. Hg. and his aqueous 20 to 30 mm. Hg. We accept the common theory that the aqueous is secreted by the ciliary processes, and we maintain that the aqueous is practically at the same pressure as the capillary venous pressure in the ciliary processes. There is nothing between these processes and the aqueous but layers of protoplasmic cells containing some 80 per cent. of water. The capillaries are enclosed by a transparent, excessively thin membrane, the capillary wall also is composed of wet protoplasm. We do not know how much water this protoplasm contains. Connective tissue and *membranæ propriæ* limit the expansion of the cell protoplasm, but we find no evidence of structure which can hold the capillaries open when

pressed on by the aqueous from outside. Capillaries elsewhere in the body are collapsed and emptied with the greatest ease by pressure applied outside—e.g., in the skin and brain. In previous investigations I found the pressure of the brain against the skull wall of the cerebrospinal fluid and the pressure in the cerebral veins was the same, and not only so, but variations of these three pressures took place together synchronously with changes produced in the general arterial or venous pressure. We maintain that the same holds good for the eye, that the pressure of the aqueous is the same as the pressure in the veins at the exit from the inside of the eyeball, and that it is practically the same as the capillary pressure.

Fig. 3 is a diagram of Mr. Thomson Henderson's, showing the eyeball, and it agrees with the opinions I have put forward concerning the

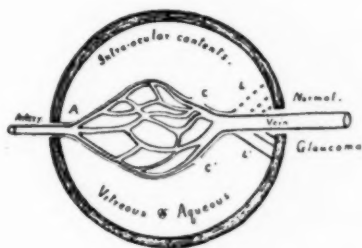


FIG. 3.

Diagram which shows that at the exit of the veins from the interior of the eyeball the venous pressure must be the same as the intra-ocular pressure. (Thomson Henderson.) L, cribriform ligament; C, iris crypts.

brain. We maintain that the pressure of vitreous and aqueous, which has been proved to be always the same, is equal to the pressure in the veins at the place of exit from the eyeball. If it was greater, the veins would be shut up. There is nothing in the wall of the veins which can support pressure from the outside. So we maintain that the pressure in all the various venous exits must be the same as the intra-ocular pressure, and the pressure therein and in the capillaries is practically identical. The least (immeasurable) difference aided by the pulse (transmitted through the contents of the eyeball) will suffice to maintain the flow from capillaries to veins. Muscular contraction of intrinsic and extrinsic muscles of eyeball also maintains capillary-venous flow as elsewhere in the body. One of the experimental proofs which we bring



forward with regard to this point is this: If we open one of the vortex veins in the eye of the cat, allow the blood to escape from there, and force Ringer's solution to run into the aqueous, by raising the pressure bottle, the outflow from that vein stops when the aqueous pressure is raised to the arterial pressure. This shows that the two pressures go up together; the aqueous pressure and the capillary pressure rise together, and when you reach the arterial pressure the outflow stops. It is the same as putting an armlet and sphygmomanometer on the arm, and gradually raising the pressure of the armlet to nearly the arterial pressure; the veins will get fuller and fuller until the pressure in the veins gets to the same as the arterial pressure, or almost the same. If the arterial pressure is found to be 120 mm., and you put on the armlet and raise the pressure within it to 110 mm., you can feel the veins getting fuller and fuller, and tenser and tenser. And we have measured the pressure in the veins, and it gets to 110 mm., that is the same pressure as in the armlet. So when we put in the fluid and raise the pressure in the eyeball, we finally stop the venous outflow, and the pressure required to stop the flow is the full arterial pressure. That is confirmed by observations made by a different method. Looking at the back of the eyeball, and watching the flow in the retinal vessels, V. Schulten found that the flow ceased, as viewed with the ophthalmoscope, when the pressure reached the arterial pressure. This shows, to our minds, that the two pressures go together, and that if you raise one you raise the other.

I now show you two photographs of cats' eyes, taken after an experiment made to-day. Afterwards I will show the actual eyes by means of the epidiascope. The experiment we did is a very easy one to perform, and very striking and interesting. We simply punctured the cornea of one side, and allowed the aqueous to escape. On then gently pressing on the belly of the cat, the iris on this side immediately burst into hæmorrhage; all the capillaries allowed blood to escape. That comes off every time. The explanation is that the normal aqueous pressure is exactly counterbalancing the capillary pressure. If you allow aqueous to escape and press the belly you raise the arterial pressure, and the capillaries at once burst, and hæmorrhage takes place into the anterior chamber. That shows that the two pressures are one and the same, the one supporting the other. The only thing we have done to the eye is to allow the aqueous to escape, and yet, on pressing the belly very slightly, hæmorrhage is produced. That explains why there is hæmorrhage in operations on and injuries to the eyeball. I do not

know whether the explanation is new to you as ophthalmic surgeons; it may be that all of you have already recognized that that is the explanation. It is perfectly clear that the aqueous no longer supports these blood-vessels, and therefore when the blood-pressure is raised they burst, and hæmorrhage takes place.

The aqueous has a distinct chemical nature, a distinct composition, and its osmotic pressure is said to be higher than that of the serum. And we know that if fluorescein is put in intravenously, as Ehrlich did, it is secreted, and appears after a few minutes in the anterior chamber, and can be seen there. That shows that some kind of circulation is going on in the aqueous. But there are records of observations which showed that if fluorescein were put in so that there was one part in 20,000 circulating in the blood, there was found one part in 400 in the urine, and one part in a million in the aqueous fluid. Therefore you see it does not get concentrated in the aqueous and the method does not show that the aqueous is being rapidly secreted and absorbed. The observations of Ehrlich are very beautiful, showing as they do the secretion of the aqueous, and the very important fact, which is known to all workers on the eyeball, that if the anterior chamber is pierced, the secretion which comes out is quite different and is far more intensely tinged with fluorescein; it is one which contains blood corpuscles, is rich in albumin, and like serum. It is a leakage secretion. So we maintain that the secretion, or absorption of the aqueous, cannot be studied in any way by opening the eyeball, or allowing the aqueous to escape, because the conditions are entirely altered. We must have a closed eyeball, with the aqueous pressure balancing the capillary as it naturally does.

I pass now to the consideration of the fluid of the eyeball in relation to accommodation. I want to deal with the transference of fluid from in front of the lens to the side of the lens, which we think is a most important point in accommodation. The pushing forward of the lens must cause transference of the liquid from in front to the side of the lens. And it is curious how little attention is drawn to that fact in any of the books which describe the mechanism of accommodation, a thing which we maintain is the most essential in accommodation. I have taken this diagram (fig. 4) from Professor Starling's excellent book on physiology which has just been published, showing Schön's view of accommodation. According to this view, the ciliary body, by the contraction of the muscle, comes down into this position, and the suspensory ligament is relaxed. How is that going to take place?

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We fail to see, because any movement downwards must raise the pressure in the vitreous chamber of the eyeball, and cause translocation of this fluid elsewhere. But there is nowhere for the vitreous to pass into, since the posterior surface of the lens does not alter. And we know experimentally that neither the aqueous pressure nor the

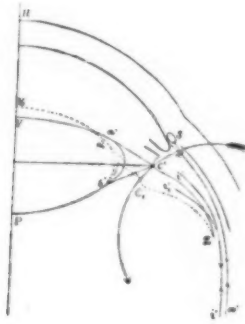


FIG. 4.

Accommodation according to Schön. The ciliary body is supposed to move into the position marked by dotted lines.

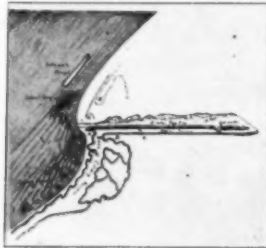


FIG. 5.

Ciliary muscle, &c., fixed in the natural position. (Thomson Henderson.)

vitreous pressure change in the least degree during accommodation. The next (fig. 5) is a diagram taken from Thomson Henderson's work, showing the ciliary muscle with the circular fibres and the meridional fibres here, acting on the cribriform ligament and the canal of Schlemm, &c. Thomson Henderson has put forward an interesting idea about

accommodation—namely, that the circular fibres of the ciliary muscle of the outer meridional fibres are antagonistic in action, and it seems likely that this is the case. Next (fig. 6) you see another of Thomson Henderson's figures; accommodation is taking place like *this*, with the ciliary body moving inwards. And Professor Starling, in his text-book, describes the same thing: the ciliary body moving inwards and forwards, and not backwards. In order that that may take place, and in order that no change in the pressure of the fluid may occur, it is obvious that fluid must pass from in front to the sides of the lens. We suggest that possibly the ciliary muscle opens up the spaces within the cribriform ligament, and Thomson Henderson has the same idea, as has also Arthur Thomson, of Oxford, who figures the same kind of thing. Possibly it opens up a passage, allowing fluid to get into the supra-

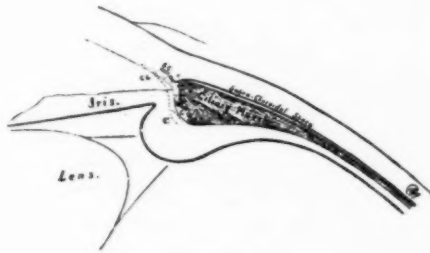


FIG. 6.

Movement of the ciliary body in accommodation shown by dotted lines. (Thomson Henderson.) The innermost fibres of the cribriform ligament (C.L.) terminate in the connective tissue stroma of the circular muscle bundles of the ciliary muscle (C), and so play the part of a check ligament.

choroidal space, which Henderson says can get filled with fluid. In whatever way it may be brought about there must be this transference of fluid, and the mechanism of accommodation is thereby co-ordinated in the most delicate way, because the transference of the least quantity of fluid can bring about instantly, in a most beautiful way, the change in the shape of the lens.

It is always said that the lens capsule and the suspensory ligament are in the eye, exerting elastic pressure on the lens, and causing it to assume its less convex shape. What is the cause of that shape? We maintain it is the intra-ocular pressure; it is the pressure in the aqueous and the vitreous maintained by the secretory action of the choroidal fringes. The expanding force is equal in all directions in the eyeball,

and this acts on the suspensory ligament and keeps the lens in its natural shape. And if you cut out the lens from the body, it increases its curvature, and why? Because it is taken from the influence of the intra-ocular pressure, and yet many people say the lens alters its shape by virtue of its elasticity. But the lens, when cut open, does not seem to have any elasticity at all; it is a soft, pudding-like body with no inherent elasticity. We say it is kept in its flattened shape by intra-ocular pressure. It alters its shape afterwards, when it is removed from that pressure. Henderson has brought forward some very

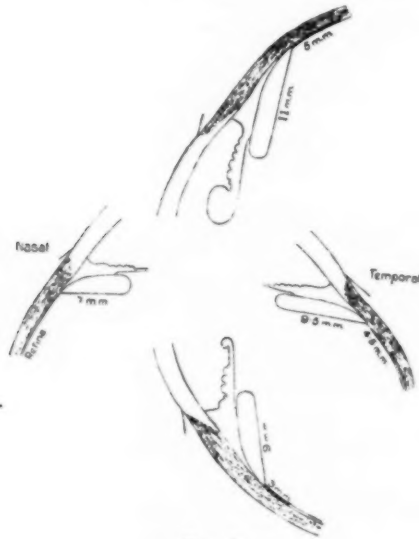


FIG. 7.

The extent of the pars ciliaris retinae in the horse's eye. On the nasal side the retina extends right up to the ciliary body. (Thomson Henderson.)

interesting figures in regard to the horse's retina. He shows (fig. 7) that it comes up much closer to the ciliary body on the nasal side than it does on the temporal side, and that if the ciliary muscle pulls up the choroid, as it is supposed to do, there is much more tissue on the temporal side which is not covered with retina than on the nasal side. There is great difference. On the nasal side such a pull must disturb the position of the retina; and that is one of his arguments against the usually accepted view. It seems to us to be a sound argument. We do not see how the choroid is going to be pulled forwards. The

eyeball is equally distended by the intra-ocular pressure in all directions, and it does not seem possible to us that the choroid should be pulled forward at all. What we think happens in accommodation is that the ciliary muscle contracts, and when muscle contracts it does not diminish in size, but it occupies the same volume as uncontracted muscle. And when the muscle contracts it moves inwards, exactly as described by Henderson, and it may also move forwards, as Starling describes in his text-book. This allows the fluid to pass from in front of the lens either into the grooves of the ciliary body, or into the spaces of the cribriform ligament, and into the supra-choroidal space. We cannot, dogmatically, say where this fluid goes, because we have not made a

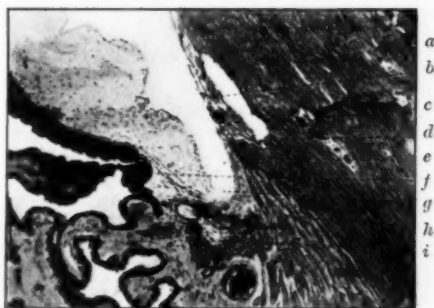


FIG. 8.

*a*, canal of Schlemm; *b*, trabecular tissue of pectinate ligament; *c*, scleral vein; *d*, dense scleral tissue; *e*, scleral process or spur; *f*, radial muscular fibres of the iris; *g*, iridial angle; *h*, meridional fibres of ciliary muscle; *i*, circular fibres of ciliary muscle. (Arthur Thomson.)

special study of the structures of the eyeball from this point of view. But we maintain that the fluid must pass from in front of the lens to the side of the lens. It must do so to satisfy the physical conditions; there is no getting away from it, and Helmholtz recognized that in supposing that the angle of the anterior chamber was deepened during accommodation. Thomson Henderson says that anatomical study will not allow of Helmholtz's idea.

The next figure (fig. 8) is one published by Arthur Thomson, of Oxford, showing the spaces in the cribriform ligament, the canal of Schlemm, and the ciliary muscle. The next is a highly magnified view showing the canal of Schlemm, and the spaces in the cribriform ligament (fig. 9).

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And into these spaces, possibly, the fluid goes when the ciliary muscle contracts. All these spaces are covered with endothelium, according to the histological investigations, and that endothelium everywhere separates the anterior chamber from the veins, and there is no direct communication. There is endothelium everywhere between, and that is a point in connexion with filtration. If you run fluid into an excised eye, these spaces are no longer supported by the blood-pressure in the capillaries and veins, and that membrane will inevitably be ruptured, because you produce positive pressure on one side and there is no supporting pressure on the other side, so the liquid will come out and get into the veins under those conditions. This delicate membrane controls the interchange, as it does in all other parts of the body, between the

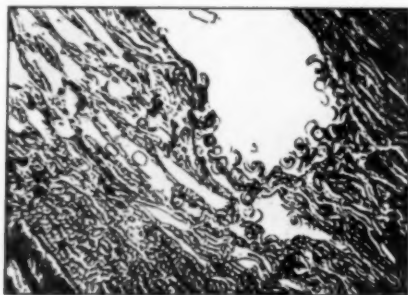


FIG. 9.

Enlarged view of canal of Schlemm and spaces of cribriform ligament.  
(Arthur Thomson.)

lymph spaces and the vessels. And if you do that experiment on the dead eye, you rupture this membrane which is only one cell thick, and so is ruptured easily, and you have conditions which do not pertain in the living eye at all.

According to Arthur Thomson there is a spur of tissue which is pulled down by the ciliary muscle, and opens a way for aqueous to escape (fig. 10). It is a pumping mechanism, the spur is pulled down, and then goes up again, as the ciliary muscle relaxes. I do not hold to the view that the aqueous is pumped out of the eye thereby, and I do not think that Thomson as an anatomist cares what function is ascribed to the mechanism; all he maintains is that the spur is there and that it is pulled down. We suggest that thereby the fluid in the front of the



lens may be brought to the side of the lens during accommodation. But how much fluid passes? One of my co-workers, Mr. F. D. Twort, has calculated this for me from the radius of curvature in the lens. He has made a careful mathematical calculation, and verified it carefully, taking the change in the curvature of the lens which is given by Helmholtz. When the convexity of the lens increases forwards, it must come in to a corresponding extent at the periphery (fig. 11), for according to the received doctrine, the curvature of the posterior surface scarcely changes. We must, therefore, accept Tscherning's view, and admit that the lens

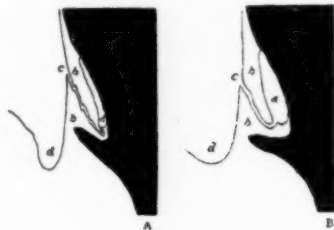


FIG. 10.

Scleral spur and pumping action of ciliary muscle according to Arthur Thomson. *a*, canal of Schlemm; *b*, the trabecular tissue of the pectinate ligament with *c*, a lymph channel, running through it; *d*, the iridial angle.



FIG. 11.

Change in curvature of anterior surface of lens. The surface at the circumference must come in corresponding to the forward bulging.

is heaped in front and flattened at the edge of the anterior surface, or suppose that the posterior surface at the edge is curved in. There must be some change, for the lens must be pressed in just as much as it is pressed out, and at the same time the aqueous fluid must pass from in front into the circumlental region. Now the actual amount of fluid which passes is calculated by Twort to be 10 c.mm., so that 10 c.mm. of fluid in front is pushed to the sides, and room for 5 c.mm. has to be obtained on either half of the circumference of the lens during

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accommodation. Mr. Donald, who is working in the laboratories of the London Hospital Medical College, has invented a most ingenious instrument for measuring drops and for dropping drops. He has brought a tube here that he has made, which will show a 10 c.mm. drop. He passes a glass capillary tube through a hole in a wire gauge of given size, and cuts it off close to the gauge-plate, and drops from that tube. He thus obtains a perfectly clean tube, fresh drawn in the flame, with a terminal diameter of given size. The size of drop depends on the external diameter of the tube. He will demonstrate a 10 c.mm. drop. There is no difficulty in supposing room sufficient for such a volume of liquid in the spaces of the cribriform ligament which lie all round the circumference of the lens. While the circular and inner radiating fibres of the ciliary muscle open up these spaces, the outer meridional fibres may act antagonistically and close the spaces. If these fibres relax on accommodation they will be bowed in by the circular fibres, and will straighten again on contraction and restore the resting condition.

Mr. R. DONALD said the size of the drop of liquid was conditioned by the periphery of the tube at the level where the drop clung round the tube. The drop came out of the point of the tube, and rose up its outer walls, so that the drop appeared transfixed at the end of the tiny dropping tube. The drop attained the precise size only under particular conditions; uniform dropping at a certain slow rate. The present tube was calibrated for one drop per second. A mercury plunger flowed regularly to and fro in the tube. He set the mercury back, placed the nozzle in the water, depressed the tube, and the mercury flowed down. Each drop here was 10 c.mm.

Professor E. H. STARLING, F.R.S.: Although I am in full agreement with most of the facts brought forward by Dr. Leonard Hill, I do not agree with him so closely as to the interpretation to be placed on these experimental results. From the practical point of view it is of more importance to know what the factors are which determine the formation and absorption of the intra-ocular fluid than to arrive at an agreement as to the theory of its production—whether, for instance, it is due to some mystical process of secretion, some intracellular changes which at present we cannot understand, or whether the mechanical processes of filtration are sufficient to account for its production. After

all, the important practical question concerns the relation of the production and absorption of the intra-ocular fluid to the circulatory conditions which obtain in the eyeball.

Some years ago I took advantage of Mr. Erskine Henderson's assistance to investigate the factors which determine the production and absorption of this fluid. The seat of its production we need hardly discuss, since it is generally agreed that the chief seat of production is the ciliary processes and the chief seat of absorption the anterior angle of the eyeball and the root of the iris. Covering the ciliary processes there is a well-marked epithelium with columnar or cubical cells. These cells are as well formed as those of the salivary glands, or of the kidney tubules, and might therefore easily be assumed to be endowed with secretory powers. Thus a priori there is no reason to question the possibility of the intra-ocular fluid being regarded as a secretion.

On the other hand, this epithelium is derived from the optic cup and is, therefore, a nervous epithelium which is no longer functional. We might consider that it had changed its function and had become a secretory tissue, or that its cells serve simply to support the capillaries and modify the filtering membrane through which the transudation of fluid into the eyeball occurs. In investigating the nature of any process we must start with a hypothesis and proceed from the explicable to the unexplained—from what we can understand to what we want to understand. We must, therefore, in the first place consider what conditions must be observed if the intra-ocular fluid is to be regarded as produced by a process of filtration from the blood circulating in the ciliary processes. In this case the energy necessary for its formation would be derived from the blood-pressure and ultimately from the heart, and not from secretory work effected by the cells covering the ciliary processes. The intra-ocular fluid in the eye is at considerable pressure; there must, therefore, be a resistance to its outflow from the eyeball, a resistance which can only be overcome by a certain pressure. But if the fluid in the eyeball is formed from the blood in consequence of the pressure of the blood in the capillaries, the pressure of the intra-ocular fluid must rise and fall with the intracapillary pressure. Professor Hill has already told you that the intra-ocular pressure varies with the blood-pressure, and this fact was well brought out in the work that I carried out with Mr. Henderson. In every case where we raised the blood-pressure in the vessels of the eyeball the intra-ocular pressure went up proportionally and remained high so long as the blood-pressure

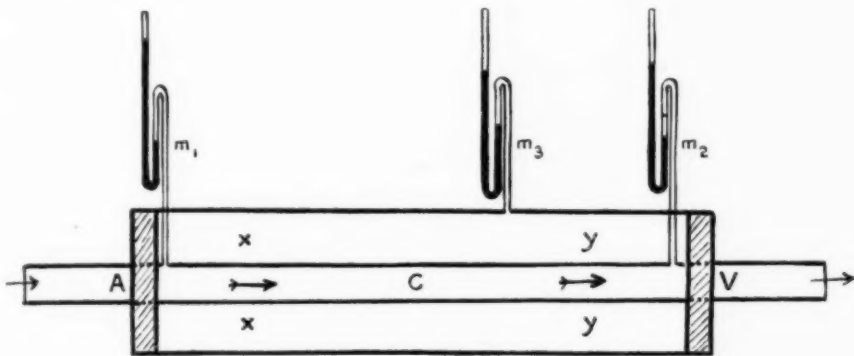
remained high. It is not merely a question of dilating the vessels by a rise of pressure and thereby increasing temporarily the intra-ocular pressure. So long as the blood-pressure is high the intra-ocular pressure remains high. On the other hand, on cutting off the blood-supply to the eyeball the intra-ocular pressure rapidly falls and the eyeball becomes flaccid.

With regard to the normal height of the intra-ocular pressure, I find it difficult to understand how Professor Hill obtained the very high figures he has given us, namely, 16 mm. Hg. to 62 mm. Hg. I have certainly obtained intra-ocular pressures approaching 50 mm. Hg., but this was with exceedingly high pressure in the blood-vessels of the eye. Ordinarily, however, the blood-pressure is much lower, and we concluded that in a normal unanæsthetized animal the average pressure would be not more than 25 mm. Hg.; and a similar figure is given by about a dozen authorities cited by Leber. I think most ophthalmologists would regard a pressure above this point as abnormally high. Not only does the intra-ocular pressure rise and fall with the general blood-pressure, but it can be shown to depend on the local blood-pressure. Thus, if the sympathetic nerve of the neck be stimulated a double effect is produced—first a contraction of the unstriated muscles of the orbit with a rise of pressure, and then, as the vessels of the ciliary processes contract so as to diminish the pressure in the capillaries there is a fall of intra-ocular pressure.

Professor Hill has stated that the pressure in the capillaries and veins of the eyeball must be equal to the intra-ocular pressure. I find it difficult to understand his reasoning. The condition in the eyeball may be roughly imitated on a model such as is shown in the diagram, where ACV is the thinnest possible rubber tube passing through the axis of a rigid glass tube  $xy$ .  $xy$  contains fluid, and fluid is allowed to pass under pressure from A to V. If the pressure in  $xy$  is greater than the pressure within the rubber tube, this collapses. If fluid is to pass through ACV it must have pressure all the way along which is somewhat greater than the pressure in  $xy$ . Now ACV represents arterioles, capillaries and veins, and it is evident that the blood-pressure in these vessels must be somewhat higher than the intra-ocular pressure as represented by the pressure in  $xy$ . The quicker the rate of flow through the vessels the greater must be the difference of pressure between A and C and between C and V, and the greater the difference also between the pressure in the elastic tube and the pressure in the space surrounding it. This difference may be of any extent until it is sufficient to burst the rubber tube.

From these considerations you will see that it is impossible to have the conditions assumed by Hill—namely, an equality of capillary and venous pressures. So long as the blood flows from C to V so long must the pressure at C be greater than the pressure at V.

There is another factor which will tend to exaggerate the difference of pressure between capillaries and veins. Since the kinetic energy of the blood in the veins is greater than that of the slowly moving blood in the wider area of the capillaries, the component of the energy moving the fluid represented by the lateral pressure of the walls must be relatively greater in the capillaries than in the veins. Thus a large flow of blood from capillaries to veins involves a considerable difference of pressure between these two points. Professor Hill has stated



that the capillaries in the ciliary processes are very delicate and would not, therefore, stand any appreciable pressure. This, however, is a pure assumption, and does not take into account the small cross-section of these vessels. Naturally, if the capillary wall surrounded a balloon a foot in diameter, it would burst at the slightest excess of pressure in its interior, but a capillary wall 3 or 4  $\mu$  in thickness, surrounding a tube with a lumen 7  $\mu$  in diameter, might be expected to stand a considerable pressure before it ruptured. Certainly a bicycle tyre in which the thickness of the wall had the same relation to the lumen of the tube would be strong enough for all practical purposes. There are no experimental facts which exclude the possibility of a considerable difference of pressure existing between the capillaries and the fluids outside them. Such a difference may be shown to exist in the connective tissue of the limbs. Many years ago, after reading

a book by Landerer on the tension of the tissue spaces, I spent several months measuring this pressure. In all cases I found that the pressure was extremely small—namely, 2 to 5 cm. of water, whereas the pressure in the capillaries might be 20 or 30 mm. Hg.

We are not justified, therefore, in denying the possibility of a difference of pressure between the blood in the capillaries and the intra-ocular fluid, and we must assume that, if the circulation is to continue, a considerable difference of pressure exists between the blood in the capillaries and the blood in the veins. The venous pressure itself must be higher than the intra-ocular pressure. If, in the model, the pressure in *xy* is raised to the pressure at V, the tube at V will collapse. As soon as the circulation through ACV is thus brought to a standstill the pressure at V will rise to the pressure at A and the circulation will go on again; that is to say, the circulation through ACV will not be brought to a standstill until the pressure in *xy* is just higher than the pressure at A; which, being interpreted, means that in order to stop the blood-flow through the eyeball naturally, the intra-ocular pressure must rise to the pressure of the blood in the arteries entering the eyeball. That does not, however, tell you what is the pressure in the capillaries of the eyeball under normal conditions; it only gives the upper limit of this pressure and does not mean that the intra-ocular pressure under normal circumstances is equal to the capillary pressure.

Assuming that the intracapillary pressure is the main factor in determining the production of intra-ocular fluid, it is important to know what is the rate at which fluid is turned out. So long as the intra-ocular pressure remains constant the rate of absorption must be equal to the rate of production. In order, therefore, to measure the rate of transudation, we must measure the rate of absorption at the same pressure. This can be determined by putting a hollow needle into the eye, filled with fluid at such a pressure that the intra-ocular pressure is just balanced, so that fluid neither enters nor leaves the eye. The heart is then cut out so that the pressure in the vessels sinks to zero. No more fluid is now being poured out by the ciliary processes, but the intra-ocular pressure is maintained at the same height as before by its connexion through the hollow needle with a reservoir of Ringer's fluid. The Ringer's fluid therefore flows into the eye, and the rate at which it flows gives the rate at which the intra-ocular fluid was being absorbed just before the death of the animal. In a series of observations made by this method, Henderson and I found that, at the normal intra-ocular



pressure, the rate of absorption was about 12 c.mm. per minute, and this is, therefore, the normal rate of production of intra-ocular fluid by the ciliary processes.

The proofs I have given you that the intracapillary pressure of the ciliary vessels is the most important factor in the production of intra-ocular fluid, and that the intra-ocular tension depends on the balance between the production as regulated by the blood-pressure and the absorption as regulated by the resistance at the anterior angle of the eye, do not necessarily imply that the intra-ocular fluid is merely a filtration. It might be that the cells were being stimulated by the blood-pressure, so that the secretion increased or diminished as the blood-pressure rose or fell. Before we can assume that the process is one of filtration we must account for the fact that the fluid, though containing practically all the salts of the plasma, is almost entirely free from protein. The slightly increased molecular concentration of the intra-ocular fluid as compared with blood plasma might be ascribed to metabolites produced by the cells. But if we assume that the capillary wall *plus* ciliary epithelium is a filtering membrane which is impermeable to colloids such as the blood proteins, there would have to be a minimum difference of pressure of about 30 mm. Hg. between the blood in the capillaries and the intra-ocular fluid for any filtration to take place at all; otherwise the blood-vessels would absorb the intra-ocular fluid. Thus the filtration theory demands not only some difference of pressure in favour of the capillaries, but that the pressure in the capillaries shall be not less than 30 mm. Hg. above that of the fluid in the eyeball. Unfortunately, we have no method at present of measuring the intracapillary pressure in the eyeball directly. It is true that there is always a considerable difference of pressure between the blood in the large arteries and the intra-ocular fluid, and the difference may be from 70 to 90 mm. Hg., but it is impossible to say how much of this pressure in the arteries is transmitted to the capillaries of the ciliary processes. It is impossible, therefore, at the present time to furnish the crucial proof of the filtration hypothesis. But the strict parallelism which exists between the blood-pressure and the intra-ocular pressure, and the fact that, with a rise of blood-pressure, the intra-ocular pressure increases, as well as the amount of fluid escaping through the anterior angle of the eye, show us the intra-ocular fluid merely as a result of balanced mechanical processes; and at the present time there is no evidence of any other processes, and we are not justified in assuming that the epithelium covering the ciliary processes acts



otherwise than passively in strengthening and modifying the qualities of the filtration membrane.

We have finally studied the conditions which alter the rate at which fluid escapes from the eyeball. Why does one not always find a permanent rise of intra-ocular pressure with a rise of arterial pressure? The association is certainly seen, but it is by no means constant. The explanation is probably found in some experiments by Henderson and myself. If we try the effect of raising the intra-ocular pressure artificially, we find that a little time after raising the pressure to 50 or 60 mm. Hg., filtration becomes more easy, as if additional channels had been opened up or pre-existing channels enlarged. A similar change might occur in the normal eye, and in this way the intra-ocular pressure might be kept at a normal height, although the arterial pressure was permanently raised. We have also tried in the same way the effect of atropine and eserine on the rate of escape of intra-ocular fluid from the eyeball. At normal pressures no difference was found between the eserinated eye and the atropinized eye.

CAT, ANESTHETIZED WITH ETHER. BLOOD-PRESSURE AVERAGE 138 MM. HG., WITH ONLY TRIFLING VARIATIONS THROUGHOUT THE EXPERIMENT.

| Intra-ocular pressure<br>in mm. Hg. |     | Rate of filtration in<br>eserine eye in cubic<br>millimetres per<br>minute |     | Rate of filtration in<br>atropine eye in cubic<br>millimetres per<br>minute |     | Rate of filtration in<br>atropine eye post<br>mortem, in cubic<br>millimetres per minute |
|-------------------------------------|-----|--|-----|---|-----|--|
| 20                                  | ... | 0  | ... | 0   | ... | 15   |
| 35                                  | ..  | 11   | ... | 8   | ..  | 20   |
| 50                                  | ... | 16   | ... | 11  | ... | 25   |
| 65                                  | ... | 23   | ... | 14  | ... | 31   |

At 20 mm. Hg. the rate of filtration was 0 in both eyes. At 35 mm. Hg. intra-ocular pressure the filtration from the eserine eye was 11 c.c., and from the atropinized eye 8 c.c., and this difference augmented as the pressure was raised to 65 mm. Hg. I believe our experiments would be in accordance with clinical observations as to the influence of these drugs on normal and glaucomatous eyes.

I might finally say a few words on one or two other points which have been raised by Professor Hill. He drew attention to the hæmorrhage into the eyeball, which occurred in the cat after letting off all the intra-ocular fluid, and then raising the blood-pressure by pressure on the abdomen. On the filtration hypothesis the normal difference of pressure between the blood in the ciliary capillaries and the intra-ocular

fluid is about 35 to 40 mm. Hg. I do not think there is any difficulty in understanding why a sudden rise of this pressure to something between 100 and 160 mm. Hg., as would occur under the conditions of Hill's experiments, should cause actual rupture of the capillaries and hæmorrhage into the eyeball.

With regard to the question of absorption from the eyeball, he pointed out that the spaces of Fontana in the canal of Schlemm were separated from the anterior chamber by epithelium. The same condition obtains everywhere in the lymphatic system. The lacteals in the villi have a continuous endothelial coat, and the endothelium of the diaphragm is continuous over the stomata, and yet particles of Indian ink or milk globules pass easily by these stomata into the underlying lymphatics. The apparently continuous endothelium does not stop the passage of fluid or even of fine particles. Filtration through it may occur without any rupture of the membrane.

With regard to the mechanism of accommodation I am unable to contribute anything founded on my own experience. The change in shape of the lens I have always assumed must be accompanied by a shifting of fluid, but this may occur easily between anterior and posterior chambers, or even between the posterior chamber and the vitreous cavity through the fibres of the suspensory ligament. The subject is not one, however, to which I have given any attention.

MR. PRIESTLEY SMITH said the subject was a large one; he would not enter on the question of the accommodation of the eye, though he would have liked to criticize what had been said, but would confine himself to one or two points connected with the physiology of the intra-ocular pressure. The pressure in the healthy eye varied in different persons, and in the same person at different times. There was no absolute normal. What was normal for one eye might be abnormal for another. The average was about 25 mm. Hg. Healthy eyes doomed to excision by reason of orbital tumour had been tested by the manometer with this result. A pressure of 60 mm. Hg., which Dr. Hill had found under certain circumstances in the eyes of animals, was much above the normal for animal and man. In the human eye it was equivalent to a severe glaucoma.

Dr. Hill maintained that the intra-ocular pressure was equal to the blood-pressure in the veins and capillaries within the eye. The speaker thought that it was equal to the venous pressure at certain points only—

viz., at those points where the veins left the eye, but that elsewhere, and especially in the capillaries which produce the intra-ocular fluid, the blood-pressure was higher than the intra-ocular pressure, which he would call the chamber-pressure. Dr. Hill's observations had shown that the intra-cranial pressure was equal to the blood-pressure in the torcular Herophili, but he had not shown that the blood-pressure in the torcular was equal to that in the veins in other parts of the skull, or in the capillaries; if there was no difference of pressure throughout these vessels there would be no movement of the blood, as Professor Starling had pointed out. In a considerable number of healthy human eyes the behaviour of the central vein of the retina close to its point of exit showed a delicate balance between blood-pressure and chamber-pressure. With each incoming arterial wave the chamber-pressure rose above the blood-pressure at this point and emptied the vein; between the waves it fell below the blood-pressure and the vein refilled; the two were in approximate equilibrium, and each in turn gained the mastery. In the majority of eyes the blood-pressure was a little the higher of the two, and the arterial impulse transmitted by the vitreous was not sufficient to empty the vein even close to its point of exit. Further from the point of exit, and especially in the capillaries of the ciliary body, the blood-pressure must be higher still.

He would like Dr. Hill's opinion as to the probable pressure in the arteries where they enter the eye. [Dr. HILL: You may take it as 100.] Taking the pressure as 100 where the blood enters, and at 25 where it leaves the eye, there is a fall of 75 mm. Hg. Where did this fall take place? It was probably not very sudden. It was important to remember the laws governing the pressure of a fluid moving through a tube. In a horizontal tube of uniform calibre the pressure falls continuously and evenly throughout. In a tube of varying calibre it is modified, and in places the fall may be converted into a rise. Where the tube is larger the fluid moves more slowly, making less pressure in the forward direction and more against the containing wall; where it is smaller the fluid moves more quickly, the forward pressure is greater, the lateral pressure less. For his own satisfaction the speaker had tested the point experimentally. A brass tube was obtained about 2 ft. long; at the two ends its diameter was equal but elsewhere it tapered like a billiard cue. Near to each end a fine nozzle was inserted into the side of the tube. By means of a rubber tube it was connected with a water tap—the thin end being the nearer to the tap. When the water was turned on and flowed through the tube a fine jet issued from each

nozzle, and the jet at the broad end of the tube played higher than that at the narrow end, although the latter was nearer to the tap; in order to make sure that this did not depend on a difference between the nozzles these were interchanged; the result was the same. In a vascular area like that of the uveal tract, the aggregate transverse section of the capillaries was greater than that of the arterioles feeding them, and this ensured a slower movement and a greater pressure in the capillaries than would be present if the transverse sections were equal; the pressure might even be greater than that in the arterioles. Professor Starling had pointed out that the capillary wall was thick enough to support such pressure, and had shown reasons of a different kind for assuming that the capillary pressure must be considerably higher than the chamber pressure—perhaps as high as 60 mm. Hg.—in order to produce the intra-ocular fluid.

It was generally stated that the ciliary processes provided the intra-ocular fluid. He thought it better to say the ciliary *body* so as to include the *pars plana*. The processes were obviously fitted by structure and position to supply the aqueous chamber; nearly the whole of their surface was in open communication with it. The *pars plana* was in intimate relation with the vitreous body. It was thickly studded with the glands of Treacher Collins. It was readily reached by staining fluid injected into the vitreous. Morbid exudation could frequently be traced from the *pars plana* into the vitreous. It seemed probable, therefore, that this part of the ciliary body secreted the fluid of the vitreous.

The tension of the eye was maintained by the intra-ocular fluid. The term "intra-ocular tension," often used by writers, was apt to confuse. When the speaker was an engineer he had learned to draw a distinction between the terms "pressure" and "tension"; the one indicated push, the other pull. We ought, he thought, to speak of the *tension* of the tunics and of the *pressure* within the eye—or of the ocular tension and of the intra-ocular pressure.

It was sometimes stated that the wall of the eye was practically a rigid case. This was misleading. The tunics were pliable, distensible, and elastic. When a finger was pressed upon the eye the wall was dimpled; the fluid displaced by the dimple was found room for elsewhere. When the finger was removed the dimple disappeared. This proved the distensibility and the elasticity of the tunics. Accurate measurements had been made to ascertain the amount of distension which occurred under a given increase of the intra-ocular pressure. Errors easily arose through lack of clear perception of such points. For example, it had

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been contended that increase in the tension of the eye was due to an increase in the pressure of the contents and *not* to an increase in their volume. But the two things were inseparable. An increase in the tension of the eye indicated an increase of the intra-ocular pressure, and it also indicated an increase in the volume of the contents, for in short periods of time neither could occur without the other.

(The discussion was adjourned until February 5, 1913.)

## Section of Ophthalmology.

February 5, 1913.

Sir ANDERSON CRITCHETT, Bt., C.V.O., President of the Section,  
in the Chair.

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### Congenital Mesoblastic Strand adhering to, and apparently penetrating, the Cornea.

By GEORGE COATS, F.R.C.S.

The subject of this abnormality is a male infant, aged 6 weeks. The left globe is microphthalmic. In a downward and inward direction a thick, fleshy mass arises in the region of the lower fornix, and passes upwards and outwards to become adherent to the cornea in its inferior internal quadrant to the extent of about one-third of the corneal diameter. The mass is covered with mucous membrane, and shows no dermal elements; it is not possible to pass a probe beneath it. The eyelids are perfectly formed, and the caruncle is present and normal. Elsewhere the cornea is clear. The pupil is displaced downwards and inwards to the seat of attachment of the fleshy mass, so that only a narrow rim of black is visible on looking in from above. The iris seems to be of fairly normal texture, but its surface is everywhere covered with a radially disposed system of fine red vessels, which form some irregular arcades near the pupillary margin.

In the right eye, which is probably of normal size, there is a superficial vascular opacity encroaching slightly on the cornea in a downward and inward direction, corresponding in situation with the adhesion in the other eye. There is a normal anterior chamber, however. The pupil is displaced downwards and inwards, and is slightly elongated vertically. Beneath it, in the usual position, there is a partial coloboma of the stroma, the pigment epithelium being apparently intact. The coloboma and the corneal opacity are not opposite each other, the opacity being farther inwards. In this eye also the surface of the iris is covered with radiating vessels having arched communications at the circulus

minor. No coloboma of the choroid could be seen, but examination was difficult.

When first seen some conjunctivitis was present, with small patches of xerosis at the limbus. There was very slight discharge shortly after birth. The child was born at term, but is small and weakly. There is a copper-tinted rash on the forehead and nose, and some nasal discharge, with excoriation of the nostrils. In the right hand the three outer fingers are fairly well formed, but joined together; the index-finger has only one joint; the thumb is large and distorted. The condition of the left hand is similar except that the index-finger is normal. The mother states that no defects are present in four other children; she knows nothing of congenital abnormalities in her own or her husband's family.

Three possible explanations of these appearances suggest themselves: (1) Inflammation; (2) mal-differentiation of the mesoblast of the foetal cleft; (3) amniotic constriction and band formation.

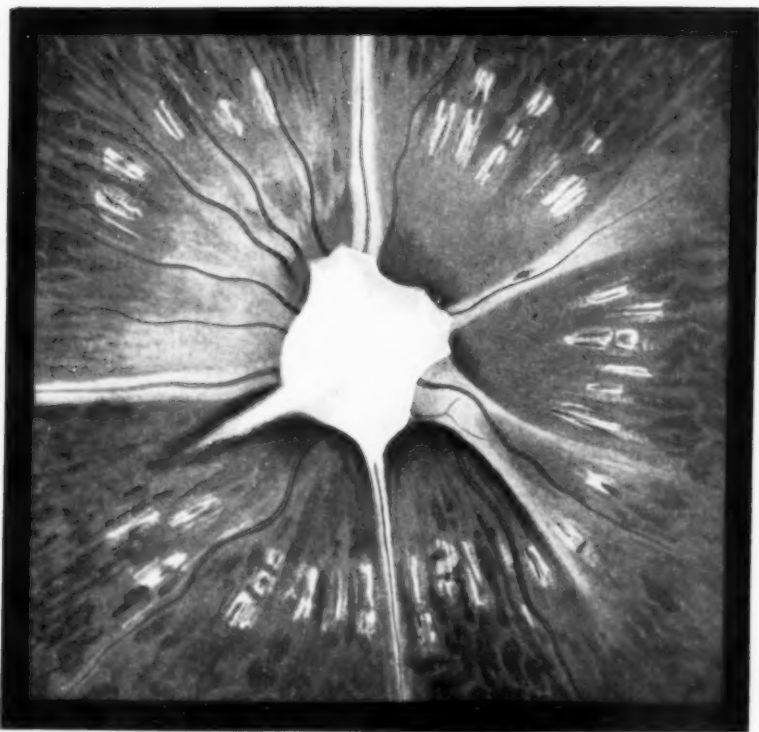
(1) This explanation would rest on the evidence of syphilis detailed above. Possibly also the very unusual development of vessels on the surface of the iris might be of inflammatory origin. In order to cause the coloboma of the right eye, however, the inflammation must have occurred in the earliest weeks of foetal life. No doubt syphilis and other noxæ sometimes cause the mesoblast to differentiate abnormally, but it is doubtful if they give rise to a true inflammation at so early a stage of development.

(2) The downward and inward situation of the strand, and the presence of corectopia and a coloboma in the other eye favour this explanation. In microphthalmic eyes colobomata are not infrequently associated with persistent mesoblastic strands. On the other hand, although there seems to be no positive reason why such a thing should never occur, I know of no recorded case in which the lack of differentiation in the mesoblast has extended through the cornea, far beyond the limits of the foetal cleft.

(3) So far as the appearance of the strand goes, this is perhaps the most probable explanation. If the amniotic fluid were unduly scanty at an early period of foetal age the amnion might come in contact with, and acquire an adhesion to, the developing eye. The superficial opacity on the right cornea might well be due to the same cause. The condition of the hands also suggests mechanical interference. V. Duyse has laid great stress on amniotic constriction and band formation as a cause of ocular coloboma, the not very infrequent







The anterior cone-like process to the left contains the hyaloid artery but this, unfortunately, is not well shown in the drawing.

*RUGG GUNN: Persistent hyaloid artery with massive white formation  
obscuring optic disk.*

symmetry of the condition being explicable by the prominence of the eyes about the time of the closure of the foetal cleft. It would perhaps be going too far to assign a preponderant part to this cause, but the possibility of its occurrence in individual cases must be conceded.

### **Persistent Hyaloid Artery with Massive White Formation obscuring the Optic Disk.**

By A. RUGG GUNN, M.B.

W. B., AGED 11, discovered about six months ago that he did not see well with the left eye. About this time he was also noticed to squint occasionally—convergent strabismus. He then recollected that twelve months before he had been hit in that eye by a tennis ball. R.V.,  $\frac{6}{6}$ ; L.V., counts fingers at 1 metre. T.n. right and left.

Examination of Fundus: Situated in front of the optic disk and obscuring it is a large white mass, roughly four times the diameter of the optic disk. It is irregular in shape and shelves steeply on the nasal side, where vessels are seen issuing from beneath it, and extending over the fundus. Several pointed, finger-like processes containing vessels extend laterally from its base; these gradually lose their white streak, the vessels continuing towards the periphery. From the anterior surface of the mass a slender cone-like process extends directly forwards. It contains vessels and terminates as a vessel in the neighbourhood of the nasal margin of the lens. Beyond the mass over three-fourths of the circumference of the fundus, a transparent, reflecting membrane gives rise to an exaggerated light reflex of the nature of a water-silk retinal reflex.

It is suggested that the condition is congenital; that the anterior process contains the remains of the hyaloid artery, and that the other processes extend along the retinal vessels. With the exception of a solitary pigment spot we find no evidence of any pre-existing inflammatory condition. The possibility suggests itself that the mesoblast in the neighbourhood of the hyaloid artery, instead of forming jelly-like connective tissue (vitreous), has in part developed into white fibrous connective tissue, which has afterwards retracted, drawing up behind it the retina with its vessels in a tent-like process.

I wish to express my acknowledgment to Mr. Rayner Batten and Mr. Kenneth Campbell for permission to record this case.

**Case of Disease in the Pituitary Region.**

By J. B. LAWFORD, F.R.C.S.

F. R., AGED 46, married, lodgekeeper. Admitted to St. Thomas's Hospital on December 23, 1912. Sight has been failing steadily for four months. R.V.,  $\frac{1}{60}$  and 20J.; L.V.,  $\frac{6}{60}$  and 20J. Oph.: Optic atrophy; O.D.'s very pale, not sharply defined; no choroidal lesions; media clear. Fields of vision show incomplete bitemporal hemianopia. Pupils react to light and in convergence; a hemiopic pupillary reaction is sometimes demonstrable.

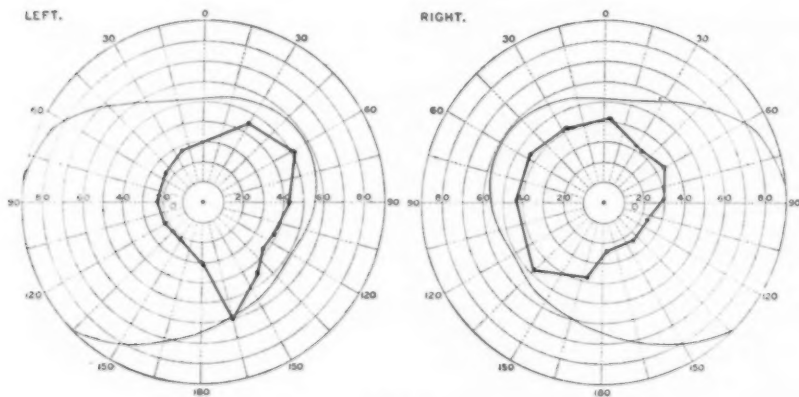


FIG. 1.

F. R., December 12, 1912.

During the last four months patient has been liable to headache of a moderately severe character, generally frontal, but not always localized. There has been no vomiting, no vertigo. Loss of sexual power for the last six months. Has always had good health. Has five healthy children; no deaths and no miscarriages. No history of syphilis. He has not noticed any enlargement of hands or feet; has not required larger boots or gloves or hat. No signs of organic disease in thorax or abdomen. Knee-jerks brisk; abdominal and other reflexes normal. Urine normal. *Wassermann test negative*. No motor or sensory paralysis. No proptosis; no interference with ocular movements. Skin not unduly dry; no loss of hair.

Dr. Turney reports that he finds no definite signs of acromegaly (apart from the optic nerve condition). Mr. Howarth reports that there is "no evidence in the nose or posterior nasal space of disease of

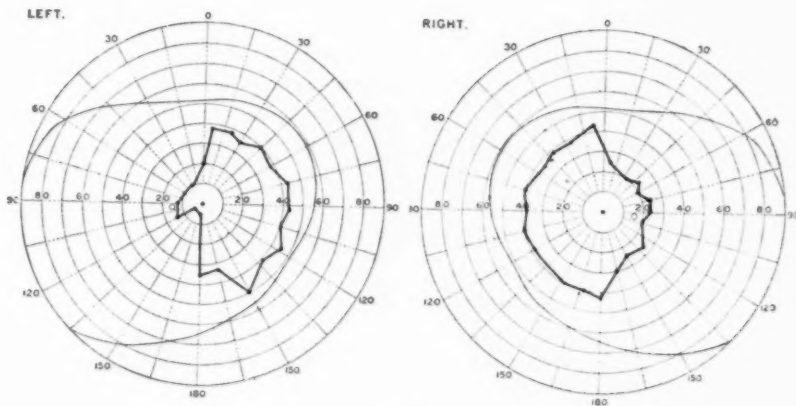


FIG. 2.

F. R., January 6, 1913.

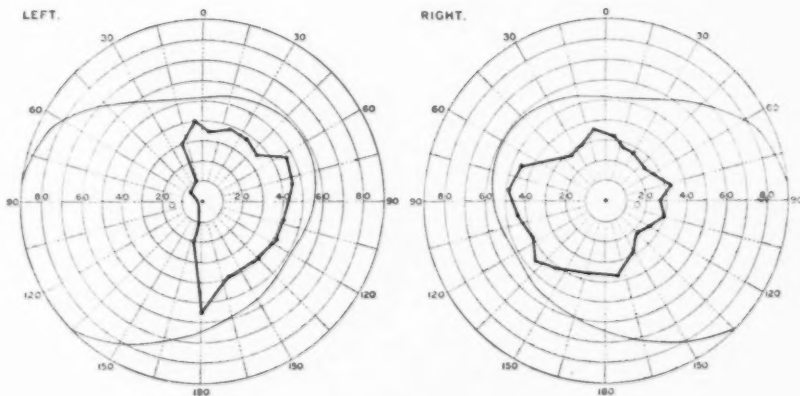


FIG. 3.

F. R., January 28, 1913.

sphenoidal or ethmoidal sinuses." X-ray examination (Mr. A. Reid) shows no noticeable abnormality of the bones at the base of the skull; the sella turcica is not enlarged nor its bony boundaries altered in shape. No appreciable loss of sense of smell.

At the present time (February 4) the condition has altered very little. The man is more drowsy than other patients in the ward; he suffers frequently from headache, usually frontal. He has been sick on several occasions; always after the administration of medicine (pituitary extract). Temperature normal or slightly subnormal; pulse rather rapid (76 to 112). Vision has deteriorated, and is now, R.  $\frac{1}{60}$ , L.  $\frac{2}{60}$ , but there has been slight improvement in the right field of vision in its temporal part. He has, however, become more awkward on moving about in the ward, in spite of his better knowledge of his surroundings.

Patient has been treated by extract of anterior lobe of pituitary body, given in 2 gr. doses once daily, and by small doses of strychnia.

#### DISCUSSION.

Mr. LAWFORD said he brought the case in the hope of obtaining opinions as to diagnosis, which offered considerable difficulty. The lesion seemed to be in the pituitary region, exerting pressure on the chiasma. There was no definite evidence of acromegaly. The man had certain symptoms which were suggestive of pituitary disease. There had been definite loss of sexual power, and he had been unduly drowsy, and suffered much from headache, usually frontal. If the case were one of disease in the pituitary region, it fell into Cushing's second group—viz., cases in which "neighbourhood symptoms" were pronounced, while general symptoms were not conspicuous. The charts of vision handed round showed incomplete hemianopia.

Mr. HUGH THOMPSON said he showed, before the Ophthalmological Society some years ago,<sup>1</sup> a case with similar fields, the cause of which turned out to be a gumma. The patient improved under antisyphilitic treatment, and the fields enlarged again to some extent, but one disk remained totally atrophic. There, however, the similarity ceased, as there was neither drowsiness nor acromegaly.

Dr. GRAINGER STEWART said two other features in the case supported the view expressed by Mr. Lawford—namely, the patient's general pallor, and the abnormally great distance between the ear and the corner of the eye. The latter was one of the signs which Cushing laid stress upon in these indeterminate cases.

Mr. LAWFORD, in reply to Mr. Hugh Thompson, said there was no evidence of syphilis in this patient, and the Wassermann reaction was negative.

<sup>1</sup> *Trans. Ophthal. Soc. U.K.*, 1901, xxi, p. 286.

**Case showing the Result of Peritomy.**

By Sir ANDERSON CRITCHETT, Bt., C.V.O., F.R.C.S.

F. A., AGED 42, professional nurse, during the last twelve years has suffered at intervals from recurrent iritis in the right eye, and from attacks of corneo-iritis in the left eye, on the numerous vessels on the cornea. On September 18, 1912, I performed an iridectomy on the right eye and a peritomy on the left eye, and the effect of the latter operation has been to place a tightening band of cicatricial tissue across the vessels. There is a partial cataract in the right eye.

DISCUSSION.

The PRESIDENT (Sir Anderson Critchett, Bt., C.V.O.) said the patient had suffered for many years from kerato-iritis—perhaps twelve years on and off. When he saw her the cornea was very vascular, as indeed was the whole eye, and the conjunctiva and sub-conjunctival tissue was very much thickened and injected. He thought the only way he could give the patient a chance was to do peritomy, and accordingly he did it under an anæsthetic. If the operation was decided upon, it should always be performed thoroughly; one should take sufficient tissue and go right down to the sclerotic; nothing should be left behind. He thought the operation was sometimes forgotten. His father read a paper on the subject over thirty years ago, and Mr. Teale, of Leeds, also alluded to peritomy as a great stand-by in chronic cases of certain types. He certainly did not regret having done the operation in this case.

Mr. T. H. BICKERTON said he could fully bear out the President's remarks. He did the operation fairly often in cases where there was much vascularity of the cornea due to gout or rheumatism—it was sometimes difficult to understand to what it was due. He also believed the operation was sometimes forgotten by medical men.

Mr. CRUISE said he was present at the operation and wished to amplify what Sir Anderson had stated. To him the remarkable feature in the case was that the infiltration of the cornea was a deep infiltration, a keratitis profunda, and the vessels were deep vessels coming from the anterior ciliary arteries, not superficial ones coming from the conjunctival vessels, which would be the ones naturally influenced by a peritomy. The improvement in the corneal condition was very striking.

Mr. RAYNER BATTEN said the operation was beneficial also in recurrent corneal ulcers, where the ulcer recurred from time to time without obvious cause. In some cases the benefit was quite amazing.



**Congenital Bilateral Deformity of Inner Canthus.**

By A. S. COBBLEDICK, M.D.

H. L., MALE, aged 39; seen at the Central London Eye Hospital. Family history: Mother, aged 60, has the same defect; one brother has a similar deformity, but to a slighter extent. He has two sisters, one of whom has a slight deformity of the same kind. Patient has four children. One boy, aged 6, has the same deformity. The deformity consists essentially of an abnormally large lacus lachrymalis, which instead of being triangular in shape is somewhat oval, so that the



Congenital bilateral deformity of inner canthus.

vertical and lateral measurements of the lacus are much greater than normal. The lachrymal papillæ are very prominent, especially on the lower lids. Associated with this condition is marked flattening of the malar bones. The palpebral fissures are small, partly on account of ptosis and partly from an abnormally short lateral measurement. This gives an appearance of internal strabismus. There is no epicanthus. Epiphora has been complained of for twenty years and is gradually getting worse. He is hypermetropic to the extent of 4.50D. Vision with correction  $\frac{6}{5}$  in each eye. Other congenital defects *nil*.

**Discussion on the Physiology of the Intra-ocular Pressure.<sup>1</sup>**

MR. MARTIN FLACK said that a perusal of the printed report of the discussion, so far, showed that Professor Starling and Professor Hill held very divergent views as to the circulatory conditions obtained in the eyeball. Professor Starling believes it to be the result of a mechanical process of filtration, and hypothesizes a difference of 30 mm. of mercury between the capillaries and the fluid outside. There is also published a schema to represent these views. But this schema is represented as without any capillary bed and therefore without the resistance due to that, so that it does not represent the conditions in the eyeball; it omits to show that the pulsatile force which is transmitted from the arteries through the wall of these vessels tends to drive fluid out of the eye. Nor, granting Professor Starling's hypothesis of filtration, does the schema represent the filtration scheme at all, because for capillaries he takes rubber, and apparently the perfusion fluid is water, and rubber is impermeable to water, whereas in the eye there are capillaries formed of wet films of protoplasm and watery fluids on either side of these. For filtration the tissue requires to be essentially a rigid wall, not the wet protoplasm films which one believes the ciliary processes to be. The same criticism as to rigidity applies to the experiment of Mr. Priestley Smith; in his trumpet the walls were of brass, and therefore the scheme did not apply. Professor Hill believes that the aqueous is a true secretion; he regards the ciliary processes as being wet protoplasmic films, and does not believe that filtration can exist within the eyeball. Professor Starling said that he found it difficult to follow Professor Hill's reasoning, and therefore he (the speaker) would like to elaborate that reasoning a little more, all the more so because a review had been published in the *Ophthalmological Review* by Mr. Erskine Henderson, which review was noteworthy for two facts: (1) That it devoted much space to the criticism of minutiae; (2) that it totally missed the whole point of the paper, which was briefly dismissed as being underlaid by the same fallacies which characterized Professor Hill's views of the circulation in the tissues and elsewhere. He proposed now to elaborate these "fallacies," as Mr. Erskine Henderson calls them. These principles were based on Professor Hill's well-known work on the

<sup>1</sup> Adjourned from December 12, 1912.

circulation in the brain; that work had now been published many years, and it had never been proved to be wrong. It was well known that on exposing the brain the brain substance bulged into the trephine hole; this bulging was circulatory in origin, for when the circulation ceased the bulging also ceased. Therefore the brain-pressure was a circulatory pressure, which was left over when the pressure due to the resistance in the arteries had been overcome—i.e., the pressure in the capillaries of the brain and pia mater. The pressure required to balance this brain-pressure, as measured by the compensation method, was the same, within the limits of experimental error, as the pressure of the cerebrospinal fluid and the pressure in the cerebral veins. The least excess over this pressure presses blood out of the capillaries. When Professor Hill talked of capillary-venous pressure he knew that it was slightly higher in the capillaries than in the venous sinuses, a slight gradient being necessary to maintain the flow; but the pressure transmitted through the wall of the capillary was equal to, not greater than, that in the veins. The venous outflow was not impeded by the pressure transmitted through the capillary wall. And since the pressure was equal to that in the brain substance, and in the cerebrospinal fluid, there could exist in the brain no force capable of producing filtration. So, too, in the eye. The eye, although not absolutely rigid, is sufficiently rigid for physiological purposes, and might more or less be regarded as a rigid box. Moreover, the skull of the child is not absolutely rigid, nor is that of a person who has been trephined, yet that weakening of the rigidity in no way interferes with the brain circulation. With regard to the eyeball itself, it had been shown by Koster that the raising of the pressure from 19 to 70 mm. of mercury increased the globe by seven-thousandths of its original volume. Thus the globe was not to any great extent distensible.

Mr. Priestley Smith argued that the eye was capable of expansion because it was dimpled by applying pressure. But he would give a simpler explanation of that—namely, that pressure forces blood from the eye, and this could be verified by the use of the ophthalmoscope. Dr. Thomson Henderson would say he could confirm that fact. Let one suppose that the pressure in the choroidal fringes was greater than that in the other cerebral capillaries, and that the cerebrospinal fluid was filtered through by this access of pressure, then this fluid, being at a higher pressure, would compress the veins and capillaries elsewhere in the surrounding parts of the brain where the pressure was lower. The only condition in the brain under which filtration could take

place was when the skull was freely opened, and the cerebrospinal fluid allowed to escape. So with the eyeball: the condition necessary for filtration, in his view, was for the eyeball to be freely opened, and then one got, not aqueous, but a different fluid. According to Professor Hill's view, the same conditions would obtain in any encapsuled organ, and in the limbs and other parts of the body. The flow of tissue fluid was maintained not by any filtration process due to *vis a tergo*, but to the pulsatile expansion and shrinkage of organs, the action of the respiratory pump, the expressive action of muscles, extrinsic and intrinsic, the effects of gravity and of posture. In the simple type of animal, the pulsatile heart stirred up fluid in the coelomic cavity, and the glands were exposed to the same pressure in their secreting and conducting parts; in such animals filtration could play no part in the process of secretion. So in the mammal, the organ or tissue was exposed to the pressure transmitted through the walls of the blood-vessels. It was sometimes urged that as the secretory pressure of a salivary gland could go above the circulatory pressure, that was a true secretion and that the aqueous was not. Professor Hill and he had examined that recently, and had shown that in such gland there was a special arrangement of basement membranes and connective tissue, which enabled the secretory pressure to rise above the arterial pressure, and the blood flow was not interfered with. But their researches showed that in the eye the blood flow was interfered with when the pressure of the aqueous was made greater than the arterial pressure. Professor Starling said—and that they could confirm from their own researches—that there might be a pressure of 5 mm. of  $H_2O$  in the tissue spaces—but he also stated there might be at the same time a pressure of 25 mm. of mercury in the capillaries. This, as the Professor said in criticism of Dr. Hill, is "pure assumption." Their experiments on tissue fluid were made by driving in a capillary needle under the skin, and measuring the pressure by the compensation method. One experiment he wished to draw attention to: The armlet of the sphygmomanometer was in position on the upper arm, and the arterial pressure having been found to be 120, the pressure in the armlet was lowered to and maintained at 115, so the blood flowed in through the arteries, but did not flow out through the veins. When the pressure in the veins taken by means of another armlet placed upon the forearm reached 100 mm. of mercury (over 1,300 mm. of water), at that time the pressure, as measured in the dorsal capillaries in the hand, was only 50 to 60 mm. of water. These capillaries could be blanched by squeezing the fist. In explanation, he

would say there were other and bigger capillaries lying more deeply, and the veins were filling up through them. Such experiments show that deductions drawn from the study of schemata cannot safely be applied to the circulation of the blood. The essential principle of the circulation was, that the heart pumped the blood into the capillaries, and that the movements of the body pumped it back again to the heart; that in the transference of the fluid by the secretory processes in the body, the controlling mechanism was the activity of the living cell, which was manifested in chemical reactions and physical phenomena, such as adsorption and osmosis, and that this secretory process was the same as took place in the formation of and extrusion of the vacuoles by the protozoa, and in which filtration could play no part. The tissue cells draw in fluid from the capillaries and secrete it by the chemico-physical forces which pertain to living protoplasm.

Dr. THOMSON HENDERSON said his views respecting the physiology of intra-ocular pressure were entirely dominated by Professor Leonard Hill's splendid work on the intracranial pressure, and therefore he maintained that the intra-ocular pressure was not a question of volume, but that, as in the case of the brain, it stood and varied with the intra-ocular venous pressure. He had not received the report of the last meeting, but he understood Professor Starling objected to that view, because it would mean that the venous pressure would be the same as the capillary pressure. Of course, such was not the case; the venous and the capillary pressures were distinct from each other and stood at different levels. The schema of the intra-ocular pressure, already referred to (*vide* fig. 3, p. 35), showed that the intra-ocular pressure was the same as the venous pressure at the point of the venous exit. The points of the venous exit were, first and foremost for the subject under discussion, Schlemm's canal. Some authors do not admit that this is a venous sinus, but as he had pointed out elsewhere,<sup>1</sup> serial sectioning conclusively proved that Schlemm's canal was a venous sinus. The other points of venous exit were the veins crossing the supra-choroidal space to pierce the sclera, and finally the central retinal vein on the disk.

The arguments in favour of the venous exit level of the intra-ocular pressure could be stated very simply. Fluids were incompressible, transmitted their pressure equally in all directions, and always tended to lie at the lowest hydrostatic level. Now, in the elastic circulatory

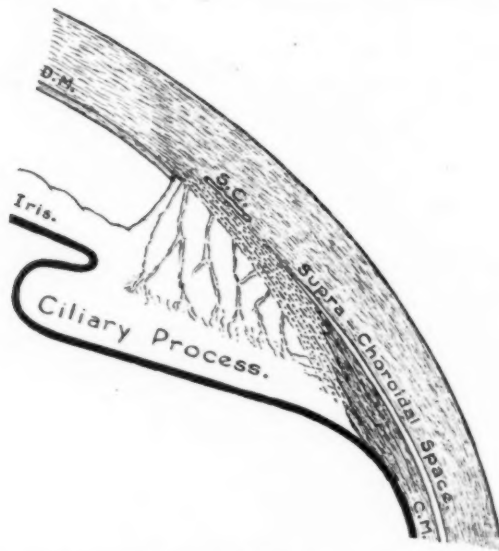
<sup>1</sup> "Glaucoma," Arnold, 1910.

system of the eye the venous pressure at the point of venous exit was the lowest circulatory pressure, therefore the intra-ocular pressure was maintained at this level, because such was the lowest hydrostatic level attainable in the eye. To put the arguments in another way, the intra-ocular pressure must be either greater, less than, or equal to the venous pressure at the point of exit. If the intra-ocular pressure of the aqueous was less than the venous pressure in Schlemm's canal, the aqueous could not get away and would stagnate. On the other hand, if the intra-ocular pressure were greater than the venous pressure, the venous walls of Schlemm's canal would be compressed. Now, although Schlemm's canal could not be observed, another point of venous exit, the central retinal vein on the disk, could be studied. By using an electric self-illuminating ophthalmoscope to observe the disk by the direct method, and at the same time applying the tip of the finger to the upper lid in the region of the external canthus, he noted that this very light touch at once caused the retinal vein, at its proximal extremity, to become shut down. If instead of using digital pressure one used a pressure gauge, as made for him by Messrs. Weiss, he found that a pressure of about 2 mm. of mercury was sufficient, in the normal eye, to produce such an effect. Now this effect was noted on a vessel the walls of which were considerably thicker than the single layer of endothelial cells composing Schlemm's canal, but, in position, both vessels were points of venous exit. Therefore, if such applied pressure sufficed to cause diminution in the lumen at the point of exit of the retinal vein, it would produce a similar effect at all other points of venous exit, including Schlemm's canal. This clinical observation showed that the intra-ocular pressure could not be a question of volume, but that the intra-ocular pressure and the venous pressure at the point of exit always balanced each other.

Professor Starling was an ardent advocate of the filtration theory of aqueous formation, and, at first sight, nothing appeared simpler. There were vessels on one side of a filtering membrane and filtrate on the other. But the theory took no note of the fact that the vessels were embedded in a loose tissue stroma, which stroma was in direct and open communication with the angle of the anterior chamber. The ciliary epithelium could not, therefore, act as a mere passive filtering membrane, because the pressure on both sides of it was the same, and if fluid did filter from the vessels, that fluid would make its way direct into the angle of the anterior chamber. He had described elsewhere the topography of the angle of the anterior chamber in man (*loc. cit.*), and had



shown why this region could in no way be considered watertight, as the aqueous passes into the supra-choroidal space as well as into the ciliary stroma. He would now merely refer to the anatomical conditions in animals. He had studied, in serial sections, the eyes of a considerable number of animals, not only all the ordinary domestic animals, but also a number of the larger mammals, as elephant, camel, lion, llama, &c. He had also done a number of injections of Indian ink and Berlin blue into the anterior chamber, but these experiments were



The angle of the anterior chamber in the cow. On the inner side of Schlemm's canal (S.C.) lie the longitudinal fibres of the cribriform ligament arising from the innermost layers of the cornea, and acting as the ligament of origin of the ciliary muscle (C.M.). The ciliary process and iris are anchored to the cribriform ligament by a series of pillars, of which the most anterior is the thickest and most developed. Descemet's membrane (D.M.) is a cuticular formation of the posterior corneal endothelium, and therefore thickens with the age of the animal. There is no barrier to prevent the aqueous at the angle passing through the network formed by the anchoring pillars into the supra-choroidal space or into the ciliary stroma. The anterior aspect of the ciliary body presents a rough, irregular surface from which the anchoring pillars arise, and which, unlike the anterior iris surface, is not covered by a layer of endothelium.

not necessary to prove that no barrier existed to the passage of the fluid in the directions named. These animals had the one feature in common that the apices of the ciliary processes lay in front of the mass of the



ciliary muscle, and thus the fact that the aqueous at the angle of the anterior chamber could pass into the tissue of the ciliary processes could be much easier demonstrated. He would illustrate as typical the eye of the cow.

The iris and ciliary body were anchored to the cribriform ligament by a series of pillars, and there was nothing to prevent the passage of aqueous into the supra-choroidal space or into the tissue stroma of the ciliary processes. The easiest escape for any fluid filtering from the ciliary vessels would be along the line of least resistance direct into the angle, and not through the double layer of ciliary epithelium. Structure and function went hand in hand, and therefore he submitted that the anatomical conditions about the angle of the anterior chamber were such as to preclude any ideas of filtration of aqueous.

If Professor Starling or anyone else would care to verify or disprove these anatomical facts, he would only be too pleased if they would come and look over his histological and zoological collection at Nottingham where he now had, in support of his statements, over 13,000 sections serially mounted.

Mr. HERBERT PARSONS said that, for various reasons, he proposed to deal only with a few points in this discussion. One reason was that he felt quite unqualified to deal with the physical side of the problem in the face of Professor Hill's and Mr. Flack's and Dr. Thomson Henderson's views. But he did not understand the extraordinary antipathy which Professor Hill and his colleagues evinced towards filtration; they seemed to him, whenever possible, to introduce some difficult method of physico-chemical influence to explain processes which were susceptible to simpler explanation. He preferred to leave those questions in the hands of Professor Starling, who was present to reply on the discussion. Moreover, some years ago he went critically into the matter and gave a résumé in his book on the pathology of the eye. Since the last meeting of the Section he had again read through what he then wrote, and he saw nothing in the discussion to induce him to withdraw or modify any serious point he then advanced. There might be some points the expression of which one might be more careful about, for just as Mr. Flack had complained of etymological inexactitude in various ways, so certain critics of his (the speaker's) work had commented in what he considered an unjust way, as for instance, on his use of the term "elasticity." He still, however, held to the main arguments he had expressed, though that might be attributed to the petrification of his critical instinct.

He thought Dr. Hill had laid unnecessary stress on the needle, and not so much on the beauty of his own needle as on the inefficacy of other people's. He (Mr. Parsons) did not think the needles which had been used by Professor Leber and Professor Starling and himself had been as bad as was suggested. Dr. Hill's needle was admittedly a very beautiful instrument, but he did not think that that gentleman had succeeded in attaining his aim. He understood him to say the sclera was a rigid box containing fluid, which was incompressible, and when Dr. Hill said "rigid" he probably meant rigid, while apparently some other people did not. That box was filled with fluid, and into it he forced a solid body of finite magnitude without losing aqueous, which seemed a difficult problem. The explanation would doubtless be that blood was forced out of the eye. If that were so, the intra-ocular pressure, being equal to the venous capillary pressure, the venous walls collapsed, and the pressure inside the globe must go up, and something must happen; either the walls must be ruptured, or the fluid must escape somewhere. The only point in which Professor Hill's work differed from that of previous observers was in the very high intra-ocular pressure he got in some experiments; and that was probably partly due to displacement of fluid by the needle. In avoiding one difficulty with extreme care, Dr. Hill had introduced another error in not allowing for the displacement of fluid by his needle. He got the air bubble at zero point before introducing the needle into the eye, and brought it back to zero immediately after introducing it. It would be noticed that the highest pressures, as set forth in the Royal Society papers, were produced with ether anæsthesia, and that might have something to do with it. In some instances the blood-pressure was stated, but not always. Another point was, that the walls of the globe *not* being rigid, unless the animal were curarized the extrinsic muscles might produce a relatively enormous effect upon the intra-ocular pressure. He believed he (the speaker) was the first to show that the increased pressure which was easily produced on stimulating the peripheral end of the cervical sympathetic was due to contraction of the unstriated muscle in the orbit. But how the fact that the extrinsic muscle pressure raised the pressure in the globe was to be explained on the theory that the walls of the globe were rigid he failed to understand. Mr. Flack's suggestion with regard to the child's skull was inapposite, because Mr. Flack had not proof that the conditions of the circulation in the child's skull were then comparable to those in the adult. Scorn had been cast on Koster's experiments, but for a globe to increase in volume 45 c.mm. with a rise of

pressure from 20 to 70 mm. of mercury was quite appreciable, and how one could contend that the volume was constant under those circumstances he could not see. He wished people would be consistent when they spoke of absorption of fluid. In Professor Hill's writings on the intracranial circulation one read of absorption by the veins, and in later publications the phrase was absorption by the capillary-venous mechanism. He did not understand what these terms implied. Absorption by the veins was spoken of in Dr. Thomson Henderson's books just as if fluid could pass through the thick walls of the veins with the greatest ease from outside. He thought secretion and absorption were fundamentally processes which were carried on by the capillaries. From the evolutionary point of view probably the earliest stage was that all capillaries performed both functions, and physical forces were utilized, as Nature usually did use them, and in some such way as the following: The filtration process in the capillaries was brought about by a vasomotor mechanism; if the arteries were dilated there was a greater intra-capillary pressure, and a process of filtration or secretion went on. If the arterioles were constricted, the intra-capillary pressure was diminished, and absorption was permitted. He did not mean to say that the utilization of such physical processes in any way eliminated the activity of the living cells which formed the filtering membrane; they had their functions to perform. That was seen in the ease with which various immune bodies passed through the capillary walls whilst others were kept back by them. These substances followed no known physical laws. Agglutinins would go through into the normal aqueous, but if the animal were immunized to a foreign blood the hæmolytic elements would not go through, except under diminished intra-ocular pressure, when the aqueous had a much larger protein content. One could, further, understand that at a higher state of development and with the differentiation of different organisms the processes might be separated, one set of capillaries performing secretion and another absorption. The work of Leber and others tended to show that the principal function of the ciliary body was that of secretion, and that of the iris was absorption. On the other hand, the supply of nutrition to the choroid, for example, was carried out by the same capillaries which took the products away. If the experimental facts were not inconsistent with a purely physical explanation, one had no right to call in other factors until one knew that the known factors failed in some essential particular. In the contribution by Professor Hill and Mr. Flack the only experimental evidence brought forward was practically a repetition

of what had been available from the work of many observers from 1850 onwards. They were at liberty to put forward any theory they wished, but it was necessary to bring forward some definite experimental evidence which was not explicable on current views, or *per contra*, they must submit evidence which upset that already adduced.

He did not propose to discuss accommodation; he did not regard it as germane to the subject, except from the standpoint used by Dr. Hill and Mr. Flack in their contributions—i.e., proving the little known from the still less known. As to the bearing of accommodation on normal intra-ocular pressure, it was a question of explaining how the process of accommodation could go on under the known conditions of intra-ocular pressure. And in the present state of flux in knowledge on the subject, he did not see how arguments adduced from the accommodation process could be of value in proving the facts of normal intra-ocular pressure.

Mr. RAYNER D. BATTEN gave a demonstration, by means of toy balloons, of the relationship of tension to pressure. He said that the ocular tension, as felt by the finger, was a mixed sensation, including, as it did, several factors—intra-ocular pressure, and resistance, the latter being divisible into two, in so far as it depended on freedom of exit of fluid from the globe, and on the elasticity of structures outside the globe, in connexion with the fluid in the globe. A third factor was the tension of the structure itself.

Ocular T, as felt by the finger, is a mixed sensation and includes several factors:—

$$T \left\{ \begin{array}{l} \text{Pressure.} \\ \text{Resistance depending on:—} \\ \quad (1) \text{ Freedom of exit of fluid contents.} \\ \quad (2) \text{ On the elasticity of structures in connexion with the} \\ \quad \quad \text{fluid of the globe, not necessarily in the globe.} \\ \text{"Tension" of the structure felt.} \end{array} \right.$$

The balloons demonstrate some of these points: The pressure in the various sections is the same, but the tension is markedly different. They also show that the tension can vary, depending on the condition of the wall, in different parts of the globe, although the pressure is the same. (1) They demonstrate that the feeling of resistance is largely dependent on the freedom of exit of fluid. (2) On the elasticity of structures connected with the fluid in the globe.

The balloon shown was a small sausage-shaped "Piladex" india-rubber balloon constricted into three equal parts by narrow bands of strapping. When inflated with air one of the sections will expand before the other two, if the supply tap is then turned off; the air enclosed in the balloons must be of the same pressure, for they connect quite freely, but the feeling of tension is markedly higher in the balloon with the thin distended walls, than in the other two thicker walled, less distended balloons.

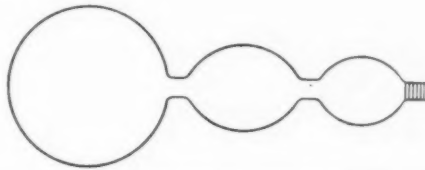


Diagram of the balloons. In the largest the walls are thin and feel tense; in the smaller the walls are thicker and feel soft.

Mr. GREEVES pointed out that an increase in the volume of the eyeball, accompanying a rise of intra-ocular pressure, could be easily demonstrated. Koster, in his experiments, took measurements of plaster casts of eyes which had been subjected to various degrees of pressure, and found definite increase in volume associated with increased intra-ocular pressure. Schulten obtained similar results by another method. He connected the eye with a pressure bottle and thus raised the pressure by known amounts, measuring the amount of fluid which flowed into the eye each time. Having lowered the pressure bottle again by the same amounts and measured the quantity which flowed out of the eye, he took the mean of the inflow and outflow as the increase in volume. He (the speaker) had done some experiments with fresh pig's eyes and got similar results. He put the eye in a bottle filled with saline and fitted with a rubber stopper, through which was passed a tube measured off in cubic millimetres as well as a hypodermic needle connected both with the eye inside the bottle and with a pressure bottle outside. Changes in the volume of the eye could thus be read off in cubic millimetres. With a pig's eye of average size, and taking the normal intra-ocular pressure as 25 mm. of mercury, the increase in size was 1 c.mm. per millimetre of mercury rise of pressure. For the first 10 mm. of rise of pressure above the normal the rate of increase in volume remained the same,

but thereafter it gradually became less. These results proved that the eyeball was not a rigid case, and that the increase in volume corresponding with even a slight rise of intra-ocular pressure was quite a measurable one.

Professor STARLING, in reply, said he thought that one of the most interesting contributions to the discussion was the little toy which Mr. Rayner Batten had demonstrated. But it had nothing to do with the immediate question, because the point brought forward by Mr. Priestley Smith and himself as to the influence of lateral pressure could only apply to moving fluids; in the case shown, however, the fluid was stationary. If one tested the pressure of that air by the manometer one would find it the same everywhere; whereas if it were taken by the fingers, as in the ordinary clinical method, or by a tonometer, the pressure in the big balloon seemed much higher than in the little one; and that showed the kind of fallacy to which one was exposed. Dr. Thomson Henderson stated that the easiest path from the capillaries to Schlemm's canal was by the connective tissue, without going into the interior of the eyeball at all. He deduced that from the anatomy; but it should be possible to prove the point experimentally. After all, these deductions from anatomy were not worth very much; they could only indicate where one must try experiments; one must not reason from anatomical considerations as against experiments. He was not himself an ardent advocate of filtration; it was not a personal question whether intra-ocular fluid was produced by filtration or by secretion by the cells of the ciliary processes; but he felt that it was a necessary condition of science that one must take the easy explanations before one should say one could not explain it. The filtration idea must not be given up until it was found the facts would not fit in with it. If the filtration hypothesis were true, the production of intra-ocular fluid should be proportional to the blood-pressure in the capillaries. And that was found to be so. He had shown that there must be a further condition; the pressure in the capillaries must be at least 30 mm. higher than the intra-ocular pressure. That was a point which might be investigated, because the difference of pressure between the capillaries and the intra-ocular fluid was conditioned by the fact that the blood in the capillaries contained protein, and it required a difference of 30 mm. between these two points, so that the protein might be filtered free from the plasma. The protein of the animal could be reduced by half by bleeding, and then only half the difference would be required to keep



the intra-ocular pressure at what it was before, so that, if the capillary pressure remained constant, the intra-ocular pressure should rise. If that did not come off, he would say it probably was not filtration; if it did come off, the probabilities were in favour of filtration.

He was glad to hear Mr. Flack, speaking no doubt in the name of Dr. Hill, acknowledge that there might be an immeasurably small difference of pressure between the capillaries and the veins. It had been contended that there was a flow of fluid from the capillaries to the veins, yet there was no difference of pressure to drive it. They now said there was a difference, and so that was a step in advance, even if it was only a little one. The magnitude of this difference between capillaries and veins was purely a question of velocity; the bigger the flow through the capillaries the bigger would be the difference. It should not be called immeasurably small because it was not yet known what it was. At this meeting an experience had been related in which the pressure in the veins of the eyeball had been measured, and been found a little above the pressure of the intra-ocular fluid. If the filtration hypothesis was right, there must be a big fall of 30 mm. of mercury between capillaries and veins. Its possibility could not be denied, but it must be proved or disproved. Mr. Flack spoke of the diagram which he (the speaker) gave in his argument last time, remarking that the rubber membrane was not a filtering membrane; but he (Professor Starling) did not say that it was. It was meant to show the mechanical feature, that to get a flow from capillaries to veins there must be a difference of pressure between them. One could as well have peritoneal membrane soaked in gelatine which would allow of a filtration of salt solution free from proteins, and the same thing would be illustrated; the main point of the argument was not affected. Mr. Flack said that if filtration took place the filtered fluid must be at a higher pressure than in the veins. But that did not follow. To get fluid through the capillaries, the pressure must be 30 mm. higher on one side than on the other if the transuded fluid contained no protein. The whole point in the filtration theory was that work was done in filtration; there must be some work to get fluid through, and when the fluid was through it had lost its energy. In Dr. Henderson's argument, he mentioned that when one looked at the retinal veins one saw that the pressure might be only a little higher than the pressure in the eyeball, because by pressing lightly on the eyeball one could obliterate the retinal veins. If the measurement was correct, it showed that the pressure in the retinal veins was only, say,



2 mm. higher than the pressure in the intra-ocular fluid. But that observation had bearing on the pressure in the vein or lymphatics, through which absorption went on, namely, Schlemm's canal. Histologists agreed that this canal was in communication with the venous system. There could not be filtration through an ordinary vein, because the direction of the tissues round the vein was concentric. If the pressure in the tissues was higher than in the vein, the vein collapsed. Dr. Hill showed that filtration occurred into the venous sinuses of the cranium, and filtration would take place into Schlemm's canal if the pressure in the eyeball was higher than in Schlemm's canal. By measuring the pressure in the retinal veins one could not tell what was the pressure in Schlemm's canal. The other point raised by Mr. Flack had reference to the general physiological question of absorption of lymph, and Mr. Flack said the lymph flow was never due to pressure, but to the pulsatile action of the organs, respiration, &c. There was one part of the body where, at any rate, one could get a lymph flow with extreme ease, and show that it varied with the pressure, viz.—in the liver. If the pressure were raised in the capillaries of the liver, a flow of lymph was produced which lasted long after the animal was dead, in fact, so long as there was a positive pressure in the hepatic capillaries.

In conclusion, he would point out once again that the production and pressure of the intra-ocular fluid was proportional to the capillary pressure in the eyeball; and if one wished to explain the production of intra-ocular pressure, it was easier to say it was filtration. If it were proved that it was not filtration, it must be assumed that the ciliary epithelial cells took an active part; they did not modify appreciably the composition of the transuded fluid, and they let the fluid pass in proportion to the pressure of blood in the capillaries of the eyeball. He believed that at the present time there were no facts which proved that the filtration theory of the formation of intra-ocular fluid was wrong.

Professor LEONARD HILL, in reply, said he believed that the prosecuting counsel ended up a trial, but he felt more like the defendant. Mr. Erskine Henderson, in a review of their work, said: "The authors of this paper, on a very small substratum of actual experimental work, came to the conclusion that all previous workers on the subject are 'hopelessly in error.'"<sup>1</sup> He was glad to have that point of view put forward so clearly, because he believed their views were right, and would be accepted finally by all, and such a statement gave these

<sup>1</sup> *Ophthalm. Rev.*, 1912, xxxi, p. 360.

the priority. He looked upon the circulation in the way which Mr. Flack had indicated—namely, that it was the function of the heart to deliver blood into the capillaries of the body—these latter were to be compared to the water-channels in a morass or bog, as they formed inter-cellular spaces or lacunæ all over the body. The heart had done its work when it had delivered blood into the capillaries; the blood was squeezed from the morass of capillaries into the (valved) veins by the action of the skeletal muscles and impelled by gravity on each change of posture. The capillaries of the hand gradually became distended on holding it down; on clenching the fist or holding it up they became blanched, showing the great effect of muscular contraction or change of posture. Mr. Parsons spoke of the influence of the involuntary muscle surrounding the eyeball; this by squeezing the eye would affect the circulation in it; so would the contraction of the ocular motor muscles and the intrinsic muscles of the eye. There was also the pull of the tissues by their chemico-physical power, pulling fluid out of the capillaries, and driving it back into the capillaries as well as pushing it along into the lymphatics. In regard to the instance given by Professor Starling of the liver in the dead animal, he (the speaker) believed it to be due to the liver cells taking up the fluid by osmotic and adsorptive forces, and pushing it along the lymphatics; he did not regard the flow as due to capillary pressure, for one knew the capacity of cells to absorb substances from the peritoneal cavity and cause a flow of lymph even after death. As Mr. Flack said, his (Dr. Hill's) work on the circulation in the brain had not been contradicted. The pressure of the brain against the cranial wall was the same as the pressure in the cerebral venous sinuses and that of the cerebrospinal fluid. A slight local excess over this pressure expelled blood out of the capillaries of the brain. What, then, was the cause of the capillary flow? He believed the flow was caused not by a large difference of pressure between the capillaries and the veins, but by the pulsatile expansion of the arteries in such a structure as the brain. With every pulsatile expansion of the arteries the pulse was transmitted through the arterial wall, and the whole brain pulsed up against the skull and that drove the fluid out of the capillaries and veins. If an artificial circulation was established through an organ and the flow was continuous, not pulsatile, the organ became œdematous. In the eye the same conditions as in the brain held good; it did not make any difference whether the eyeball was absolutely rigid or not, as long as it limited expansion of the fluid volume within; the cerebrospinal cavity was not absolutely rigid—e.g., there was the occipito-atlantal ligament.

The conditions of the cerebral circulation held good, in the child with a membranous anterior fontanel, or in a man and animals whose skull had been trephined and the opening closed by a membrane.

In such an organ as the brain and eye, when the arterial pressure rose and expanded the arteries, the limits of expansion were quickly reached, and more blood in the arteries could only obtain by diminution of blood in the veins, or expulsion of cerebrospinal, or aqueous, fluid. Diminution in venous volume occurred, and this converted the vascular system of the organ into a more rigid system with a rapid rate of flow, and the blood pulsing out of the veins. With regard to the capillary pressure, Professor Starling had maintained that it must be 30 mm. of mercury higher than that of the aqueous, so as to maintain filtration against the osmotic pull of the proteins. He (the speaker) would not agree that this phenomenon, as studied outside the body with dead membranes and serum, was of the same order as inside the living animal, because he thought that the living conditions could not be reproduced. He would not accept, without argument, Professor Starling's 30 mm. of mercury difference, but for his present contention he was willing to accept the 30 mm. difference. Professor Starling said it must be 30 mm. higher for filtration, and suggested an interesting experiment. Mr. Flack and he had already tried it, and the following were the figures obtained. He knew how open-minded Professor Starling was, and that this was only a matter of trial, so that some day they would be in agreement. There was no prejudice in this discussion, and the aim was to get at the truth. In the cat experimented upon the arterial blood-pressure was 140 mm. of mercury, and the aqueous pressure 40.5 mm. Hg. as measured with a needle with a large hole in it, which went in very well. The moment the needle was opened in the eye, the compensating bottle was being run up, so very little fluid could escape and drive the air-bubble index outwards; the compensation was done too quickly. To the finger the pressure in this eye felt no higher than in the opposite eye, and he maintained that such readings were correct in cats under ether narcosis and with a blood-pressure of 140 mm. Hg. They took away 50 c.c. of blood from this small cat (weight 255 gm.), and put in 50 c.c. of Ringer's solution. After that the blood-pressure was 125, the intra-ocular pressure 35 mm. After that the animal was bled again to the extent of 30 c.c., replacing it with 30 c.c. of Ringer's solution. Then the blood-pressure was 70, the intra-ocular pressure 25. There were not quite the conditions which Professor Starling would say there ought to be; he would say that the arterial

pressure ought to be got to 140 again, and then see what the intra-ocular pressure was. But there was no evidence of the intra-ocular pressure being distinctly raised by the substitution of salt solution for blood. If the blood-pressure fell from 140 to 125, we should expect the intra-ocular pressure to fall from 40·5 to 35. [Professor STARLING : Put in more Ringer, and analyse the plasma.] Another experiment had been carried further since the last meeting ; and they laid great stress on it in proof of their views. He had mentioned what happens on letting out the aqueous fluid : the iris comes forward and touches the cornea, and sometimes commences bleeding spontaneously. If it did not bleed, it would on gently pressing the animal's belly. Professor Starling explained that by saying there was a great difference between the capillary pressure and the atmospheric pressure. But after the aqueous was let out, if one felt the eye it would feel soft and boggy—every ophthalmic surgeon would agree with that. There was no feeling to suggest tense vessels in the eyeball. And if one had the needle in the eye and allowed the aqueous to flow out and the iris to come forward and it spontaneously started to bleed, and the bleeding point were watched, and the pressure bottle were raised and fluid again run into the anterior chamber, the bleeding was found to be stopped by a pressure of about 10 mm. of mercury. So whatever vessel was bleeding was not at a greater pressure than 10 mm. of mercury. It was probably less, because to obtain a sudden visible cessation of the hæmorrhage one raised the pressure more than necessary. He maintained that that was like the capillary pressure which one would get elsewhere, but by the vital secretory power of the eye the capillary pressure was raised to 30 or 40 mm. of mercury. Of course, the pressure in the eyeball varied with the arterial pressure. The secretory pressure of the ciliary body controlled the pressure by varying the relative volume of aqueous and blood, but if the arterial pressure rose more blood came into the eye, the arteries dilated, and the veins were constricted, and so a compensatory amount of room was made. In this way there was more blood in the arteries, less in the veins, a higher pressure pertained in capillaries, veins, and aqueous fluid, and so the intra-ocular pressure was raised. He did not think that, because the pressure in the eye went up with the arterial pressure, it showed that it was a question of filtration.

Professor Starling mentioned last time an experiment which he had made of putting a needle into the eye and measuring the inflow of fluid after cutting out the heart. He (Professor Hill) could not understand the experiment as a legitimate one, because the animal was dead and

the circulation stopped. When the fluid began to run in, blood was running out of the eye, pressed out by the fluid. The canal of Schlemm was covered by thin endothelium, unsupported by blood or other liquid on one side under the conditions of this experiment, and fluid pressing in from the needle was bound to rupture it, and then filtration occurred. But there was no proof that aqueous fluid escaped from the eye by filtration in the normal conditions when the venous vessels were full of fluid and at the same pressure as inside the eye. The conditions of the experiment were abnormal. They had been asked to accept the filtration hypothesis at present, because it was a simpler one; but he could not see that it was. He could not find a filtration membrane when he examined the structures under discussion. There was nothing like a rigid membrane, with greater pressure on one side than on the other. Even supposing it was filtration, the nutrition and pressure of the eye were governed differently from other tissues, and its pressure was kept higher to make it a perfect optical instrument. What was it that kept the eye in a condition different from that in the tissues around? Why should it be kept permanently tense in all states of health and yet the tongue not be kept tense in the same way? If it were not the living secreting cells of the eyeball which kept it like that, what did keep it? If it was the circulation which controlled filtration and absorption in the eye, one had to come back to the vasomotor centre and locate the vital quality there. It was much simpler to suppose that the eye by its inherited vital power controlled the intra-ocular pressure and circulation. The cells were acting in a vital manner, not by mechanical means, such as filtration, at all.

With regard to capillary pressure, and what it was, he would draw attention to some experiments. If one placed the web of a frog under the microscope and examined the circulation, one saw the flow going through the arteries with the greatest velocity in the deeper layer of the tissue, but in the superficial network of capillaries and veins it was slow; one could see separate corpuscles moving through the capillaries. If the heart of that frog was ligatured, the circulation did not at once cease, but went on for thirty seconds or a minute, after which it stopped in all the vessels except a few. Sometimes in a vein and the capillaries opening into it the flow would go on for some time. In one such case the flow persisted twenty minutes after the heart had been tied, and not differing much from the normal speed. And if, when the flow was ceasing, one touched the leg, one got a flow in that vein by very little alteration in the position or pressure on the limb. Roy and Graham

Brown had found that an external pressure of 20 mm. of water sufficed to diminish the size of a vein; Roy compressed the web or mesentery with a bag of transparent peritoneal membrane, which he distended with water, pressing the vascular membrane against the microscopic slide, and watching it with the microscope. Twenty millimetres of water-pressure sufficed to narrow the vein, and after the animal was dead a pressure of only 5 mm. of water caused the blood to flow out of capillaries and veins. Similarly he (Dr. Hill) had found that a very slight pressure, nothing like 30 mm. of mercury, would determine the blood flow in the capillaries after ligature of the heart. It took a great pressure to overcome the resistance in the arteries, where the flow was rapid and the vasomotor system came into play; but he thought it needed only the least difference of pressure to cause the flow out of the capillaries into the veins.

With regard to Mr. Greeves's experiments on the dead eye, it must be remembered that the dead eye had lost its blood; the dead eye therefore could be expanded somewhat by pressure of fluid because it was not full of blood; and naturally for the first 10 cm. of mercury its volume would be increased more than subsequently because up to 10 cm. it was being filled up to its normal living condition. And the same could be said of Mr. Priestley Smith's experiment of dimpling the eye, for one thereby pressed blood out. The balloon experiments were very interesting, and he thought the probable explanation was that the rubber wall was several layers thick in the smaller bags, and thus the rubber wall could be more easily distended elsewhere by the pressure of the finger, and felt flaccid. These experiments had no bearing on the discussion except to throw doubt on readings of eye-pressure obtained by the tonometer.

He considered their salivary gland experiment very important, because it proved that in the salivary gland the saliva could rise up to a much higher pressure than that in the carotid artery. If the duct were obstructed, one could get a pressure of 200 mm. of mercury, while in the carotid artery the pressure was 150. When they opened the vein coming from the salivary gland under those circumstances they found blood did come through the salivary gland, and as the secretory pressure rose it came quicker and quicker. The reason was that each little salivary alveolus was surrounded with a *membrana propria*, which they believed to be a very strong rigid structure. The salivary cells pulled in the fluid by their physico-chemical powers from the capillaries, and the fluid began to distend the alveoli when the duct was obstructed,



and the veins were then narrowed, and following that the pressure rose in the veins and capillaries; and then the vascular system in the gland became more like a rigid system of tubes, and the flow of blood became quicker through this rigid system. The secretory pressure could not obstruct the veins, because the *membrana propria* became tight, and acted in the same restraining manner as the leather of a football did on the contained bladder. In the case of the eye, he believed the ciliary processes were secreting fluid, pulling it out from the capillaries, and there was nothing to stop the pressure of this fluid acting on the capillaries of the iris, ciliary body and retina, and so the pressure could not rise above that of the veins within the eyeball without stopping the circulation. Professor Starling said the capillaries could stand great pressure without rupturing, because of the thickness of their wall in comparison with their diameter. He (Dr. Hill) had not questioned that: his point was to ask what could the capillary wall do in standing a pressure exerted from outside? There was nothing to hold it open. There could not be a pressure of aqueous outside greater than the pressure inside, otherwise the vessel would be shut up. He believed the capillaries and tissues to form a boggy mass—i.e., protoplasmic substance with lacunæ bounded by colloidal films and the whole permeated with water.

He did not feel that he was a good exponent of his own views; he tried to visualize what went on inside the living eye, but did not think he was a success at making, by means of words, others see what he believed he saw himself. He hoped that by further experiments the important problem would be settled, one way or the other; and if any members would go down to his laboratory and see the experiments he had described, he would be only too pleased to show them.

*Note.*—Mr. Henderson, in his review, says: "The authors' statement about the nature of glaucoma, and the *modus operandi* of operative treatment, is unsupported by any evidence. What the tissue lymph is to immunize, and against what must be left to the imagination," &c.<sup>1</sup> In regard to this criticism, Professor Hill and Mr. Flack say that glaucoma is due to some nutritive error in the eye, secondary to degenerative changes which interfere with the circulation, or otherwise caused. The essential point of an operation is not to relieve intra-ocular pressure, but to produce an adequate flow of tissue lymph, and so relieve the nutritional error.

<sup>1</sup> *Ophthalm. Rev.*, 1912, xxxi, p. 363.



## Section of Ophthalmology.

May 7, 1913.

Sir ANDERSON CRITCHETT, Bt., C.V.O., President of the Section,  
in the Chair.

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### Case of Exenteration of the Orbit, with Partial Excision of the Maxilla and Ethmoid for Rodent Ulcer.

By N. BISHOP HARMAN, F.R.C.S.

THIS is the most serious case of the kind I have seen, and it rather calls to mind the specimens preserved in museums from the days when this disease was apparently allowed to go untreated and to eat its way deeply into the face. In this case, however, there has been no lack of treatment; on the contrary, there has been a great deal of it, and the patient is the worse for some of it.

The patient is a woman, now aged 54. In 1896 (i.e., seventeen years ago) she noticed a small pimple on the right cheek just under the eyelid. She noticed that it scabbed. She treated it herself, at one time with acetic acid, at another with solid caustic. This she did whenever the lump reappeared.

In 1905 she came to hospital with a rodent ulcer nearly as big as a farthing. X-rays were then the vogue for rodent, so she was treated in this fashion. There was an apparent cure, but the ulcer returned again and again and was repeatedly treated with the rays during four years. On each recurrence it covered a slightly larger area than before. The woman says that "even when it had gone from the surface she could feel it thick under the surface."

In 1909 zinc ions were to the fore, so she was transferred for this form of treatment. For a short time it reduced the surface appearance of the growth to two small nodules as large as rape seeds; but the whole speedily recurred with a good deal of irritation.

In 1910 she was sent for radium treatment, which she had under the very best auspices. She had ten months' assiduous treatment. Then she was sent to me with the suggestion that the growth should be excised.

In 1911 I saw her myself for the first time. She had lost the whole of the lower lid, and there was a rodent ulcer nearly as big as a penny piece, and it was fixed to the maxilla. There was a slight loss in the mobility of the eye due to the dragging down of the conjunctiva, and some irritation of the conjunctiva and cornea, probably owing to exposure. The eye itself was healthy, and had a visual acuity of  $\frac{6}{18}$ . It was obvious that the condition required immediate and very thorough excision, possibly also the removal of the eyeball. I removed the whole of the growth, stripped off the periosteum from the subjacent bone, and finding a deep ingrowth towards the lachrymal sac that structure was removed. The tissue immediately below the eye was examined, but appeared quite healthy. Portions of the periosteum and the tissues left in situ were snipped off for microscopical examination. No growth was found in these fragments. The main growth was typically rodent ulcer.

A large graft was prepared on the left forearm, and so soon as it and the wound were ready the graft was stitched to the face. This attempt to form a new eyelid was not, however, successful; the position of the bandaged arm rendered sleep almost impossible to the patient, so the attempt had to be abandoned. The wound healed well, and contracted to a fairly small area, but there ensued the disadvantage that the globe was depressed by the scar, and the eye had to be covered to get rid of the diplopia.

The patient was seen periodically, and all seemed well until September, 1912, eighteen months after the removal of the ulcer. The woman then said she felt a numbness about her cheek and upper lip; and it was evident that the partial mobility of the eye that had remained after the operation had been lost. The eye was fixed in extreme subduction. There was also a suggestion of a nodule at the inner extremity of the upper lid in a region where there had been no growth before. She was taken into hospital. An incision below the eye showed an abnormal organized tissue, and not merely shrunk scar tissue. A piece of this was examined microscopically, and found to be rodent ulcer with a particularly well marked formation of cell nests.

The woman and her husband were told of the seriousness of the

condition and the necessity for an extensive operation. The possibility that they might like to try radium again was suggested, but most emphatically rejected.

The operation performed was as follows: An incision was made  $\frac{1}{4}$  in. wide of the old scar, right round the side of the nose, and along the margin of the upper lid so as to include the lashes. The skin of the upper lid minus the lashes was turned up, and the whole of the contents of the orbit turned downwards. Every obstruction was severed, including the optic nerve at its foramen. The mass of the contents of the orbit were thus turned out with the growth and the cavity of the orbit left clear. The bones were next examined, and since there was a suggestion of rottenness about the maxillary and ethmoid surfaces, the whole of the inner and lower walls of the orbit were removed. The orbital plate of the maxilla was found to have depending from it a mass of growth rather suggestive of a wasp's nest. The cavity left after this procedure was enormous; orbit, nose, and antrum were opened into one. The cavity was loosely packed with gauze, and cleansed and dressed daily. The patient made an excellent recovery, and the great cavity gradually shrank until now it would not receive an undersized walnut. She syringes it out daily, and it causes no trouble, except that the exposed mucous membrane seems particularly sensible to weather changes. The passages of the nose are exposed to view in a very striking manner, and it is possible to see their relations in a manner that is rare.

It has been suggested to me that I should close the opening with a graft. But I do not propose to do this. For my part I prefer that the region of the growth should be left open for inspection in the most complete manner possible. And the patient on her part would not entertain for one moment the idea of again undergoing the torture of the constrained position necessary for a graft from the arm, for she has nothing to spare from her face. The cavity is now lined above with the upper lid, which has stretched considerably, and below and on the inner side with clean, moist mucous membrane. I propose to have a small mask made and painted to represent eye and eyelids, and if this be fixed to well-fitting spectacle frames every purpose will be served.

The case points a moral. That no treatment can compete with cold steel for the radical cure of rodent ulcer. When these little scabbed pimples appear they can be removed with definiteness, and certainly within a few minutes, and no noticeable scar will be left. There is

no such certainty and definiteness to be obtained by any other mode of treatment. Of all forms of treatment, other than the knife, carbon dioxide snow is in my experience the best: far better, quicker, more certain and infinitely less expensive in time and appliances than X-rays, radium, or ionization. But good as carbon dioxide snow is compared with these other three, I for one feel that there is never that certainty in the extinction of the growth when the snow is used as when there is the clean sweep of a sharp knife. If this woman had had the ulcer excised when it had attained the size of a farthing, it is practically certain that at this date she would have had a sound face, two good eyes, and complete freedom from the horror of a big hole in her face and the daily necessity for careful dressing. The moral of the case is that before we recommend our patients to be treated with this or that clever form of treatment, we should point out to them the possibility of failure, with the likely succession of a worse estate, and at least put before them the superior advantages of five minutes with a sharp knife.

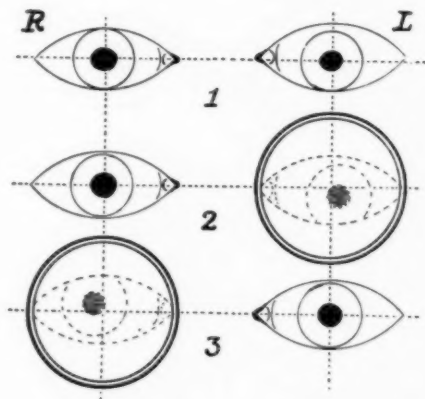
### **Case of Extreme Hyperphoria ; Operation by the New Subconjunctival Reefing Method ; Cure.**

By N. BISHOP HARMAN, F.R.C.S.

THE patient is Mrs. E. K. K., aged 28. She was sent to me by Dr. George Arthur, of West Ealing, in October, 1912. His letter stated that the patient complained of severe headache, usually on the left side, that came on almost immediately on using the eyes for near work. He had examined the eyes, and found a moderate degree of astigmatism, the correction of which improved vision. But he considered the real trouble was due to a serious defect in muscle balance, the correction for which was: Exophoria  $2^{\circ}$ , hyperphoria  $15^{\circ}$  prism over left eye base up. He suggested that I should operate if the case was considered suitable.

The following are the notes of my examination of the patient. They confirm the findings of Dr. Arthur. The eyes are deeply set. Cornea small, only 10 mm. diameter. Fixation binocular. General ocular movements excellent. The left upper lid has a usual level of 1 to 2 mm. higher than the right. The pupils are slightly oval horizontally, and the right is larger than the left. When one or other eye is covered the latent squint is at once manifest. It can be seen very well by covering one eye with a piece of thin ground glass; immediately the covered eye is

seen to diverge. The diagram shows the position assumed by the covered eye. If the left be covered the right continues to fix, and the left turns down and slightly outwards. If the right be covered that eye turns up and out, whilst the left continues to fix. It was also noticed that covering the left eye did away with the unequal lift of the left upper lid. Refraction: R.V.  $\frac{6}{24}$ ,  $\frac{6}{18}$  attempts;  $-0.5D$ . sph. and  $-1D$ . cyl., ax.  $20^\circ$ , D.O.  $\frac{6}{6}$ . L.V.  $\frac{6}{12}$ ;  $+0.5D$ . sph. and  $-1.5D$ . cyl., ax.  $20^\circ$ , D.O.  $\frac{6}{6}$ . Muscle balance: With the diaphragm test two distinct and entirely separate images were seen one above the other, and slightly separated laterally. The vertical separation was greater than that allowed for by the scales supplied with the instrument, which run up to  $6^\circ$  prism.



(1) Both eyes open, binocular fixation. Pupils slightly oval horizontally, right slightly larger than left; left upper lid slightly higher level than right. (2) Left eye covered by disk of satin glass. The latent squint becomes manifest, right eye fixes, left eye turns down and out. (3) Right eye covered, squint manifest, left eye fixes, right turns up and out.

Fixation was with the right eye by preference. With  $8^\circ$  prism base up over the left eye (in addition to the correcting glasses noted above) the error was corrected, so that she could read the ordinary small print reading card of the diaphragm test. There was some exophoria but of inconstant degree, and that was easily remedied by carefully centring the glasses when the hyperphoria was corrected. For distance vision the test was made with the Maddox rod. Then a balance could only be obtained with a  $14^\circ$  prism, but gradually this could be reduced to  $12^\circ$ .

The difference between the hyperphoria manifest in the near and

far tests seems anomalous. But it is accounted for when the conditions of the two tests are recognized. With the diaphragm test the position is that naturally assumed in reading, which in this case favoured the presumably weak muscle. This difference in the tests, the greater readiness of the right eye to fix when looking through the diaphragm test, and the upward lift of the left eyelid when both eyes were uncovered, led to the conclusion that the *left superior rectus* was at fault. This tendon was either too long or inserted too far back, so that it worked at a disadvantage. The additional effort required of this muscle to bring up the eye to the proper level was reflected in the overaction of the levator palpebræ superioris, a muscle which is developmentally one with the superior rectus. Operation was obviously the correct treatment, for glasses providing such high degrees of prisms as would correct or nearly correct the defect would be unsatisfactory owing to the unpleasant phenomena they cause of bulging walls, &c.<sup>1</sup>

November 7 (operation): Local anæsthetic. Left superior rectus reefed 4 mm. The prominent overhanging eye made the approach to the tendon somewhat difficult, and the reefing forceps could not be used; the tendon was therefore reefed with the aid of two squint hooks. The reef was secured on each side, and the stitches brought forward and inserted into the sclera close to the limbus before being tied. No anchor-stitch was used. The technique of the operation was that described last year.<sup>2</sup> The operated eye was bandaged, and the patient allowed to be out and about as usual.

November 14: Stitches removed. With the Maddox rod there was an over-correction requiring a prism of 2° to 4° base up over the right eye to correct it. There was some irritation at the scleral site of one of the stitches; this stitch was of black silk, and the dye was not fast; a small marginal ulcer formed, but cleared speedily with treatment.

December 11: Tested for balance on near and far vision, with the diaphragm test and Maddox rod; there was orthophoria under all conditions. The patient has had no more headaches since the operation, and can read with comfort.

February 26, 1913: Orthophoria perfect. The scar at the site of the operation is of the slightest. It is now noted that whereas before the operation the left upper lid was on a slightly higher level than the

<sup>1</sup> Harman, "Judgment of Size and Distance of Objects," *Trans. Ophthal. Soc. of U.K.*, 1904, xxiv, p. 297 (footnote).

<sup>2</sup> Harman, "A New Operation for Squint: Subconjunctival Reefing and Advancement," *Trans. Ophthal. Soc. of U.K.*, 1912, xxxii, p. 246.

right, the reverse is now the condition; the left lid is a trifle below the level of the right. It is probable that this is the effect of relieving the nerve of the left superior rectus of the excessive work that it had to do before the tendon was shortened, and which caused overaction in the levator muscle.

March 11: She was examined by half a dozen ophthalmic colleagues prior to her return to Greece. Perfect orthophoria was found.

### A Case of Double Tubercular Iritis.

By EDGAR CHATTERTON.

THE patient, a boy, aged 15, came to the Western Ophthalmic Hospital on March 18, 1913. He first noticed that the sight was bad thirteen months ago, since which time it has been getting worse. There has been no pain. With the exception of some enlarged glands below the angles of the jaw he is in good health, and shows no sign of tuberculosis.

The family history on both sides gives no evidence either of tuberculosis or of syphilis. When first seen there were numerous yellowish vascular nodules of the iris of both eyes, occupying, for the most part, the angle of the anterior chamber. There was much "keratitis punctata," several posterior synechiæ, and a considerable amount of vitreous opacity, preventing an examination of the fundi. R.V.  $\frac{6}{36}$ , L.V.  $\frac{6}{36}$ .

On March 25,  $\frac{1}{3000}$  mg. tuberculin (T.R.) was injected and repeated every week. The right anterior chamber has been tapped several times.

On April 29 the right vision had improved to  $\frac{6}{24}$ .

There is now (May 7) marked improvement, the nodules, especially in the right eye, being less prominent and smaller, two of them having nearly disappeared. The "keratitis punctata" is considerably less.

I am indebted to the courtesy of Mr. Kenneth Campbell for permission to show the case.



## A Case of Ocular Torticollis.

By SYDNEY STEPHENSON, C.M.

E. L., AGED 13½, has been under observation since August 23, 1905.

History: First child. Born at term, without instrumental aid, after a natural labour. There was nothing wrong with the baby at birth. When aged about 6 weeks the baby developed whooping-cough, which lasted for several months. During recovery from that ailment the child was noticed to hold his head in an unusual position. So far as can now be ascertained, this came on at the age of 2 or 2½ months. A photograph taken at the age of 2 years shows that the torticollis is well developed. The child was taken to several hospitals, and eventually to the Queen's Hospital for Children, where I first saw him. The mother (an intelligent woman) has noticed that when the child's head is crooked there is no squint, but that when the head is straight the right eye turns up and out.

Present state: The head is turned towards the left shoulder at an angle that varies whilst under observation from 10° to 40° (fig 1). There is also slight rotation of the head, so that the face instead of being turned towards the right shoulder, as it would be in an ordinary case of torticollis, is turned towards the left shoulder. There is no tension upon the sternomastoid muscle. The face shows no particular asymmetry. The left eye "fixes," and with the head awry there is a very slight, almost imperceptible, upward deviation of the right eye. When the head is straightened (which can be done without the least difficulty by the patient) the right eye develops an obvious upward squint (fig. 2), and when the head is carried over to the right shoulder the squint becomes still more pronounced. In the first position the mirror-reflex lies just below the centre of the right pupil; in the second position, near the lower edge of the pupil; and in the third position, on the lower part of the cornea, altogether below the pupil. The secondary deviation of the left eye is downwards. Diplopia when the head is straightened, but not when it is crooked. R.V. (corrected),  $\frac{6}{12}$ , iv letters. L.V. (corrected),  $\frac{6}{8}$ , iii letters. No. 1 Jaeger with each eye.

Note by Mr. E. E. Maddox.—Born with defective development of the left superior rectus, learning in a few weeks how to unite the eyes. The suddenness and largeness of the deviation of the right eye, when

the head is held erect, is due to its being a secondary deviation. He holds his head so as to make the least call on the left superior rectus, and then sees single. For some reason he has always preferred to use his left eye, in spite of its weak muscle; perhaps this vision is better. Advancement of the left superior rectus 1 or 2 mm. might be all that is needed. I think the vertical diplopia greatest up and to his left, the highest image belonging to the left eye, and extorted.



FIG. 1.

FIG. 2.

Case of ocular torticollis.

#### DISCUSSION.

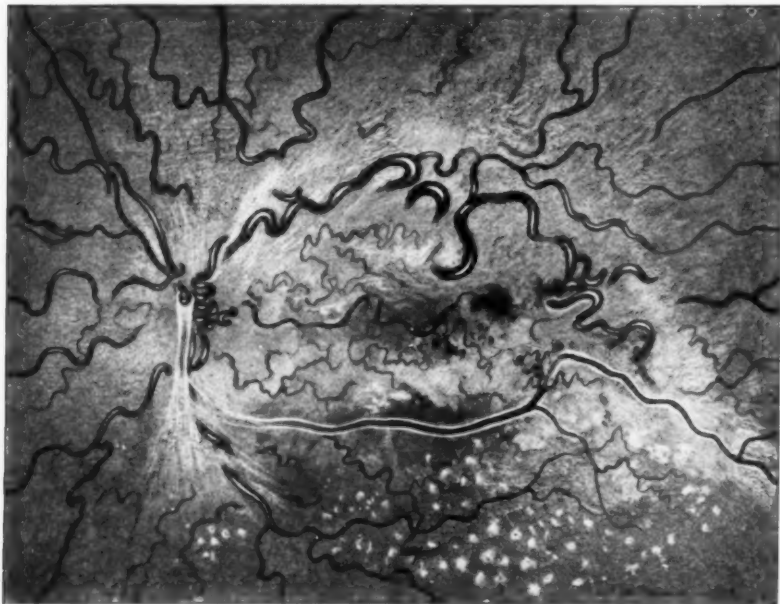
Mr. STEPHENSON added that the most simple explanation was that either as a result of a congenital condition, or perhaps as a consequence of whooping-cough, he developed paralysis of one of the extrinsic muscles of the eyeball, with squint and diplopia. He discovered that he could do away with the diplopia by holding his head in the constrained position, and this became stereotyped, and had remained so to the present time.

The PRESIDENT (Sir Anderson Critchett, Bt., C.V.O.) said he thought the explanation given by Mr. Stephenson was correct. One knew how usual it was for children with strabismus and kindred conditions to take the easiest way out of their difficulty, and no doubt this boy did so.

**Exudation of Retina with Dilated Vessels.**

By HAROLD GRIMSDALE, F.R.C.S.

H. A., AGED 17, knows his eyes had good vision a year ago; noticed left eye defective for three months. R.V.,  $\frac{6}{3}$ ; L.V., hand shadows at 2 ft. There are several groups of dilated vessels over fundus. The



Massive exudation with dilated vessels.

disk is the seat of a rosette of large vessels, apparently of new formation, while from the disk run up and down large dilated vessels; from the outer side of the disk is a vessel lying flat, with thick white walls. There are numerous patches of exudation and hæmorrhages over fundus.

Mr. GRIMSDALE said he had seen the case for the first time only two days previously. He regarded it as an inflammatory condition: there were large areas of inflammatory exudation, and vessels entering it. Running from the disk was a vessel with thickened walls, flat and tortuous, instead of being raised up. The boy said that he was able six months ago to see well, and that the failure of vision dated three months back.

## Two Cases of Angioma of the Retina.

By G. H. POOLEY, F.R.C.S.

*Case I.*—Mrs. C. History: First seen by me on June 20, 1910 (sent by Dr. Banham), when her vision with a considerable amount of hypermetropic astigmatism was  $\frac{6}{12}$  in the right eye and  $\frac{6}{24}$  in the left. A note made of the left eye says, "Bands in the vitreous behind the lens which branch freely, and can be traced to the optic disk. There are numerous fine vitreous opacities in the left and some in the right eye." The vision of the right eye gradually improved until in July of the same year it was normal. The sight of the left eye did not improve. In January, 1912, I was able to see the left fundus more clearly, and was struck by the large size of the retinal vessels. Both the upper and lower temporal vessels were very much enlarged and very tortuous. On tracing them outwards I found that after passing above and below the macula respectively they formed a series of angiomatous swellings at the outer periphery of the fundus. These are connected together by branches, some of which connect two angiomatous masses together, thus forming a plexiform angioma. There are at least five masses to be seen which vary considerably in size. On the peripheral side of the angiomata are large areas of choroidal degeneration or colobomata. Subsequent history: In March, 1912, the sight of the left eye had improved up to  $\frac{6}{12}$  partly. Since then the sight has steadily deteriorated, until in June, 1912, it was only  $\frac{6}{60}$ , and in March of this year it was only  $\frac{3}{60}$ . There has not, however, been much change in the condition of the fundus.

*Case II.*—As a contrast I now show a case of angioma which I showed at the Ophthalmological Society in 1910,<sup>1</sup> which consists of a single mass and which has undergone practically no change since the time I showed it. The description of the single mass is practically the same as that of the plexiform one; the difference being: (1) two distinct sets of retinal vessels are involved in the second case; (2) the number of the angiomata and their intercommunicating vessels; (3) the presence of areas of choroidal degeneration or colobomata on the peripheral side of the angiomata.

It is interesting to note that I first saw both these cases on the same day.

<sup>1</sup> *Trans. Ophthal. Soc. Lond.*, 1910, xxx, p. 238.

**Case of Giant Cell Sarcoma of Upper Lid.**

By G. H. POOLEY, F.R.C.S.

MRS. P., aged 65. Seen by me at the Royal Infirmary, Sheffield, on September 24, 1909. There was an oval pedunculated swelling on the right upper lid, mobile on the deeper structures, and not firmly fixed to the skin over it. This occupied the region of the middle three-quarters of the upper lid, and extended up on to the forehead for about  $\frac{3}{4}$  in., as well as backwards into the orbit. It was elastic to touch, with some pseudo-fluctuations; the skin over it was bluish, and the vessels injected. Superficial to it was a scar, which the patient informed me was the result of an operation performed at the hospital at R— in May last. She informed me that an incision had been made and a piece of fat escaped. The sight of each eye was  $\frac{6}{6}$ ; the right eye moved freely, but was displaced downwards. As I had been so fortunate as to have seen two cases before—the first, one of Mr. Grimsdale's patients at St. George's Hospital, and the second, one of Mr. Poulett Wells's patients at the Central Eye Hospital, which is described in the *Transactions of the Ophthalmological Society*, 1901, xxi, p. 97, I had no hesitation in advising the wide removal of the tumour as it was probably a sarcoma.

On September 27 I made two incisions on her forehead above the tumour—one reaching from the middle line above the nose and above the eyebrow, to the external angular process of the orbit; another one at right angles to it extended upwards about 1 in. on to the forehead; I also made a lower crescentic incision below the eyebrow, joining my first at its extremities, so as to remove all diseased skin with the tumour. I found the tumour to be definitely encapsuled; it was easily removed; it extended deeply into the orbit, and was wrapped round the tendon of the superior oblique muscle, from which I was able to separate it with the blunt dissector. As the tendon moved quite freely and did not appear to be involved I removed the mass, keeping as close to the orbital roof and the conjunctiva as possible, and removed everything between except the ocular muscles. The removal was effected mostly by the blunt dissector. I was able to close the skin wound after suturing the deeper structures with catgut. Recovery was uneventful, and she left the hospital on October 21. The tumour was examined by Professor Beattie, who reported: "Very definite myeloid sarcoma;

the tumour contained small round cells and very numerous giant cells." I saw the section myself; it was so very like a typical myeloma that I believe the specimen was used for teaching purposes. Other parts of the tumour consisted of round cells. Portions were sent to Dr. Andrewes, of St. Bartholomew's Hospital, and to Mr. J. H. Parsons for confirmation; they consisted of round-cell sarcoma. The ocular movements were perfectly good after the operation.

On December 7, 1909, her sight was reduced to  $\frac{6}{36}$  by the presence of vitreous opacities. On November 15, 1910, she returned with a recurrence of the growth. The right eye was now pushed down, and there was marked proptosis. Ocular movements were free except for some limitation in an upward direction; there was also some ptosis. She was again admitted, and on December 5 I performed exenteration of the orbit, removing the lower wall of the frontal sinus and part of the outer wall of the orbit, as well as the periosteum on the nasal side of the orbit. Recovery was uneventful, and she left the hospital on January 7. She remained well until May 9, when she was very ill with pleurisy.

On November 21, 1911, she was admitted again with a recurrence in the scar on her forehead, and I removed the recurrence as thoroughly as possible. Since then there has been no further recurrence. The microscopical examination of the two recurrent tumours showed typical round-cell sarcoma, of which Professor Beattie has kindly furnished me with a report.

All three cases which I have seen have been in women of later middle life; they have all commenced in the centre of the upper lid; they have all been definitely encapsuled, and the first two, so far as I know, did not recur. This last was a recurrence when I first saw it, and each recurrence has seemed more malignant than the original growth. This case does not seem to fall in with any of the three classifications given by Mr. Mayou in the *Transactions of the Ophthalmological Society*, 1910, xxx, p. 97, and I remember that the report on the case at St. George's Hospital said "definite round-cell sarcoma." This case, like Mr. Ormond's, reported in the *Transactions*, xxx, p. 107, showed recurrence, but, unlike his, the recurrence was local, unless it proves that the attack of pleurisy was due to a neoplasm; as, however, this has greatly improved, I cannot be certain whether it is so or not.

The literature of these cases has been so well described by Messrs. Wells and Mayou in vol. xxx of the *Transactions* that I do not think any further attempt on my part is necessary.

**PATHOLOGICAL REPORT BY J. M. BEATTIE, M.D.**

Lying below the epithelial surface there is a definite tumour area which is composed of fibro-cellular tissue. The fibrous tissue is well formed, but at certain areas the cellular character of the tumour predominates. The cells are largely spindle-shaped and mononucleated, but lying among them are numerous large, irregular cells with a homogeneous cytoplasm, and with numerous nuclei. These cells correspond in all their essential features with the osteoclasts of bone. The blood-vessels throughout the tumour are imperfectly formed, most of them showing merely an endothelial coat. At places yellowish-brown granular pigment is seen mainly in the supporting tissue, but also in the tumour cells. This is so marked at places as to suggest melanotic sarcoma. The general character of the growth and the presence of the myeloplaxes corresponds with the structure of the myeloid sarcoma seen in the jaw, femur, and other structures.

The PRESIDENT remarked that the present method of exenteration in these cases was one of the greatest advances which had been made in modern days in ophthalmic surgery. He remembered the time when the only method in vogue was to get away as much of the growth as possible with scissors and otherwise, pack the orbit with a very strong caustic paste, such as Vienna paste, and trust to Providence that it would burn out most of the growth. Sometimes, as in a case which was recorded by Mr. George Lawson, the whole of the orbital bones came away; and he believed that specimen was still in Middlesex Hospital Museum. The difference between the intense suffering which was caused by the horrible caustic and the comparative immunity from pain by the present method marked another great advance in the humanity of the operation.

**Oculomotor Paralysis with Rhythmic Spasm.**

By H. HERBERT, F.R.C.S.

THE following case is one to which I referred at the meeting of this Section last November.<sup>1</sup> In order to avoid needless repetition, the report is mainly supplementary to the account of Mr. Greeves's case, shown in November. I bring up the case, apparently the twelfth recorded, chiefly with the object of suggesting a partial explanation of the condition.

<sup>1</sup> *Proceedings*, p. 23.



In all the previous eleven cases there was paralysis, complete or incomplete, of the whole of one third nerve (both third nerves in one instance), so far as voluntary impulses and normal associations were concerned. And there were involuntary, regularly recurring contractions of certain muscles supplied by the nerve. In all there was vigorous spasm of the pupillary sphincter, and probably in all of the ciliary muscle also, though this was not always definitely determined. In five of the patients there was synchronous elevation of the upper lid, changing a moderate ptosis to practically normal opening of the palpebral aperture. And in five there was some slight inward movement of the eyeball at the onset of the spasm, reducing (abolishing in Greeves's case) the existing divergence.

My patient is now an otherwise normal youth, aged 19. The present condition of the right eye is said to have existed without appreciable change since the age of 3 months, when it was first noticed. About ten or eleven years ago an operation was performed upon the right upper lid for ptosis. The patient exhibits the palpebral, pupillary and accommodation phenomena. The palpebral aperture remains normally open for about fifteen seconds. This is succeeded by drooping of the lid for about twenty-five seconds, the change being often preceded by slight twitching of the lid. Then the lid is raised again, and the alternation is repeated. The timing observed on several occasions has been nearly constant, though susceptible of temporary alteration (*see below*). As the lid goes up the pupil contracts rapidly to a width of about 1.5 mm. During the ptosis period the pupil enlarges slowly and gradually to about 6 mm., at which it remains for a short time before the next onset of spasm. Retinoscopy shows the ciliary muscle to undergo rhythmic contraction similar to that of the pupillary sphincter, changing the refraction to the extent of about 3D. The changes go on constantly during sleep. According to the mother's (unconfirmed) observations on a few occasions recently, the periods of lid elevation and depression during sleep are more nearly equal than those given above.

On examination the whole of the third nerve is found to be more or less paralysed. There is no voluntary action of the levator palpebræ. There is almost no upward movement of the globe, and inward and downward rotation are very restricted. The pupil shows no reaction to light except a slight twitch obtainable quite at the beginning of the dilatation period. There is no lid-closure reflex. Convergence affects the pupil to some extent, but not the pupil alone. With strong convergence the contraction period of all the three muscles — lid, pupil, and accommodation — is somewhat lengthened. The relaxation period is shortened, and the dilatation of the pupil is less marked, for a few cycles. Strong efforts at elevation and at adduction of the globe have a similar effect, the adduction efforts being especially effective in this respect. Abduction tends to shorten the contraction period somewhat.

These indirect effects of voluntary impulses, reported of other cases also, are curious, since direct volition has no influence upon the spasm cycle. The fourth and sixth nerves are normal.

This patient differs from all—except, perhaps, one<sup>1</sup>—of the others in showing no divergence. There is the same absence of strabismus (except when the patient attempts to look upwards or downwards), as is seen in congenital paralysis of the sixth nerve. There is thus no scope for the inward movements reported of other cases. Tested with the mirror in the dark room, convergence is normal during the spasm periods, and good up to about 2 ft. during the relaxation periods. Correspondingly, the corrected vision with -1.25D. cylinder is  $\frac{3}{8}$  nearly.

The rhythmic spasm, different from anything seen elsewhere in the body, appears to require a local explanation. As regards the two presumably constant features—the contractions of pupil and of accommodation—there is no difficulty. As pointed out to me by Dr. Jacob, of Nottingham, the nerve-fibres here concerned belong to the autonomous system. In this system, as in the sympathetic, ganglia lie in the course of the nerves, forming breaks in the continuity of the neuron. Each nerve cell in the ciliary ganglion with its nerve-fibre marks the commencement of a second neuron, which, cut off from central control and inhibition at a very early age, has evidently remained healthy and vigorous. The powerful regular rhythmic discharge seen in the pupillary contractions, each rising rapidly and dying away slowly and gradually, followed by a brief interval of rest, is characteristically vegetative. Dr. Jacob would attribute the synchronous normal raising of the lid to spasm of the unstriped levator muscle, innervated by the sympathetic. The implied overaction of the muscle, like that seen in the pupillary sphincter, may be simply the uncontrolled discharge of energy accumulated during the period of rest.

A similar explanation will not hold for the inward movement of the globe at the onset of the spasm, recorded in five cases. Here we have to deal with the cerebrospinal nerve system and with striated muscle. There are no ganglion cells interposed between the nucleus and the termination of the nerve-fibres. And the comparatively feeble restrained movement contrasts with the vigorous action seen in the

<sup>1</sup> Levinsohn, *Zeitschr. f. Augenheilk.*, 1907, xvii, p. 341. In this case it is not stated that there was divergence, and there was no inward movement at the onset of spasm. The vision was, however, defective—viz.,  $\frac{1}{2}$ .

unstriated muscles. Here there is merely the correction, partial or complete, of existing divergence. In Greeves's case, where the movement was possibly the most pronounced, it reached "the middle line." If this was tested by the mirror in the dark room, it means that convergence became normal during the spasm periods up to the distance at which the test was made. Whereas in my case (and possibly in Levinsohn's case) convergence is nearly normal throughout, in the other cases convergence acted mainly or only in conjunction with spasm of accommodation and of pupil, thus preserving the normal association of these three functions. The power of convergence was too much enfeebled to act independently of its normal associations. Thus the inward movement of the eye is obviously one of convergence, and not of adduction, as it has been regarded.

If, as is supposed, this one-sided lesion be a nuclear one, and if the centre for convergence lie across the middle line, very small variations in the extent of the lesion suffice to account for the clinical variations seen—namely, convergence either practically normal, or enfeebled on the affected side, or abolished on the affected side. For a nuclear lesion, the published accounts show a remarkable absence of variation in extent. The uniformity with which the whole nerve, and nothing but the nerve, has been affected, is suggestive rather of a basal lesion. In the incomplete paralysis apparently no portion of the nerve has entirely escaped, while there has been no spread across the middle line (except in the one complete double lesion) or to other nuclei of either side. But some of the accounts have been too imperfect, more especially as regards convergence, to assist much in indicating the site of the lesion.

### **Case of Arterio-venous Communication in the Cavernous Sinus successfully treated by Ligature of the Common Carotid.**

By J. HERBERT FISHER, F.R.C.S.

MRS. M. A. S., aged 54, saw me at St. Thomas's Hospital on March 5, 1913. Eight days previously, after doing a day's washing at her daughter's house, she felt giddy and fell on the back of her head. She remained at her daughter's house for the night, having been unconscious for a short time. On regaining consciousness she complained

of noises in her head, and was also sick. She returned to her own house the following evening, making a journey by tramcar and walking unaided. She also remained in bed the following day, and the noises in her head were worse when she was lying down.

On the morning following her fall the left eyelid began to droop, and this progressively increased. When I first saw her—eight days after her fall—on the left side there was complete ptosis, partial mydriasis, complete paralysis of the third nerve, but some evidence of activity of the fourth and sixth cranial nerves. The left eye was somewhat proptosed: there was slight œdema of the ocular conjunctiva: no other cranial nerve was involved. On examination pulsation of the left eyeball could be both seen and felt, and with the stethoscope a systolic bruit was distinctly audible over the left eyeball, forehead, and temple. Compression of the left common carotid artery at once arrested the noises heard by the patient, and also the pulsation of the globe. The patient had always hitherto been a thoroughly healthy woman. The vision in the affected eye was  $\frac{6}{18}$ . An X-ray examination was made, but threw no additional light upon the case. The blood-pressure was found to be 145 mm. Hg. The urine was normal. The protrusion of the œdematous ocular conjunctiva gradually increased, and all voluntary movements of the eyeball ceased. The bruit was also found to be audible over the left lateral sinus. The soft tissues of the lids gradually became more tense, and some supra-orbital pain was complained of. Compression of the common carotid artery diminished both these symptoms. The patient was kept in bed absolutely. Ophthalmoscopic examination was not easy in the earlier stages, but it was obvious that there was some slight distension of the retinal veins. No hæmorrhages were discovered.

On March 18 the common carotid artery was ligatured by Mr. Sargent at the site of election. The patient came round quietly after the anæsthetic without vomiting, and there has never been at any time the smallest disturbance of the cerebral functions. Pulsation of the eyeball was completely arrested from the date of application of the ligature, but one week after the operation the same noise was audible to the patient as before, and the faint blowing systolic bruit could be heard with the stethoscope. Two days later the bruit was inaudible both by the patient and the observer, and it has not returned. The patient was kept in bed until April 20. The left pupil had by this time become equal in size to the right and some movements of abduction, and wheel-like rotation effected by the superior oblique muscle, were beginning to return.

May 7, 1913: Some further improvement in the movements is slowly but progressively taking place. Ophthalmoscopic examination is still difficult. No hæmorrhages or retinal exudates can be discovered, the veins appear rather dark and full, and the retinal arteries are inconspicuous, being probably darker in colour and smaller in size than the normal. Direct vision is at present not better than  $\frac{6}{24}$ ; the field to hand test is of good size. The pupil varies in size from time to time, but does not yet respond to light stimulus. The lower part of the ocular conjunctiva protrudes between the lid margins as an œdematous roll which is diminishing, though very slowly.

#### DISCUSSION.

Mr. ELMORE BREWERTON suggested that in such cases the internal carotid was the vessel which should be tied, and that a greater percentage of cures would result if this were done, and also the chance of cerebral trouble afterwards would be lessened. He believed that the blood-pressure in the circle of Willis was better maintained by tying the internal carotid rather than the common carotid. In the latter case a leak might be established, and blood would come down the internal into the external, and so the brain on that side would not be well nourished. If the bifurcation were low down in the neck, the natural impulse would be to tie the internal carotid, and he suggested that the common carotid was selected because the surgeon found it easier to tie.

The PRESIDENT remarked that a case on all fours with that described by Mr. Fisher would be found in the *Ophthalmic Hospital Reports* thirty-five years ago; the case was under the care of Mr. Hulke, who tied the common carotid with an equally good result to that obtained by Mr. Fisher. Still, there was much in Mr. Brewerton's suggestion.

Mr. POOLEY said he had now a similar case under his care, and he hoped soon to report the result of tying the internal carotid.

Mr. HERBERT PARSONS said there were a number of similar cases on record, and those who were interested in the subject appeared to have overlooked the collected cases by de Schweinitz and Holloway. Here the recorded cases were collated, and the different methods of treatment discussed. His memory was that they were rather unsatisfactory, as in course of time there was recurrence of pulsation, whatever had been done.

### An Unusual Arrangement of Opaque Nerve-fibres.

By ERNEST CLARKE, F.R.C.S.

J. S., AGED 12, saw me in November, 1912. Right eye: With -3D. sph. and -0.5D. cyl., axis 30°, V. =  $\frac{9}{16}$ . Left eye: "Has never seen properly" with this eye: with -20D., V. =  $\frac{9}{16}$  part. The left fundus shows the extraordinary picture figured by the plate. The arrangement of the opaque nerve-fibres forms a convex ring round and partly encroaching on to the disk, giving a crater-like appearance which is intensified by the centre of the disk being deeply cupped (*see Plate*). The opaque nerve-fibres spread from all parts of the disk, but chiefly on the outer side and involve the upper portion of the macular region. The retinal vessels bend over the steep ring which surrounds the disk, and as they pass on to the surrounding retina are in parts covered by the nerve fibres. The case presents a remarkable resemblance to that of a girl depicted by Mr. Sydney Stephenson in the *Ophthalmoscope*, 1905, vol. iii, p. 169.

#### DISCUSSION.

Mr. A. HUGH THOMPSON said that with plus 10D. one could see a number of glistening crystals in the vitreous. He asked whether that was considered to have any connexion with the opaque nerve-fibres or the high myopia, or whether it was merely fortuitous.

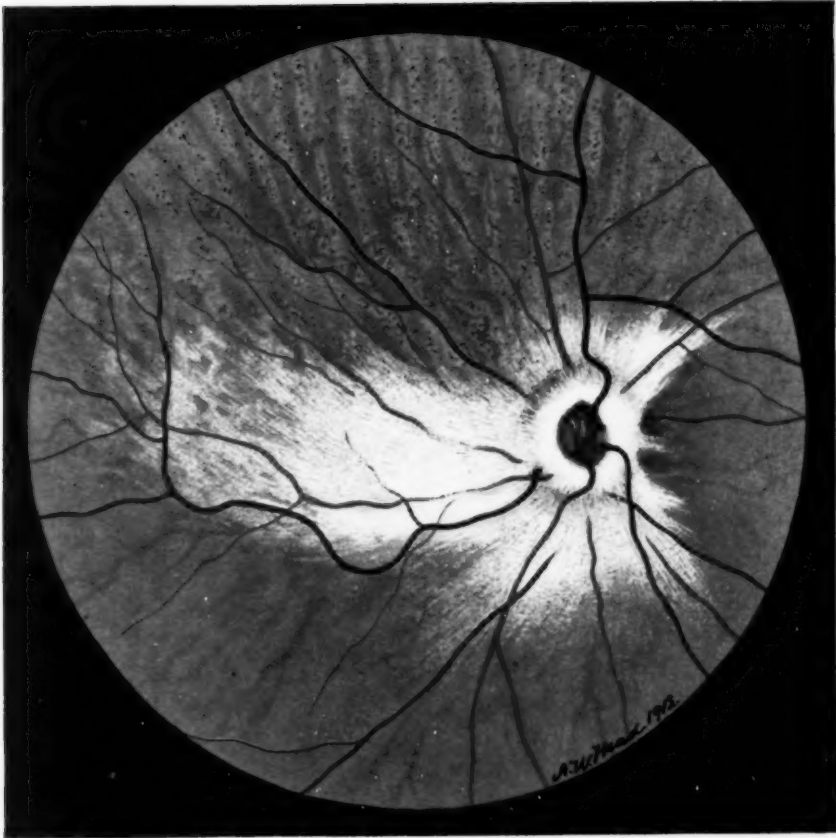
The PRESIDENT commented on the remarkable completeness of the ring, which he had not observed before, though he had seen one or two cases in which it was partial.

Mr. ERNEST CLARKE replied that he regarded the glistening crystals as accidental.

### A Subconjunctival Drain after Trephining.

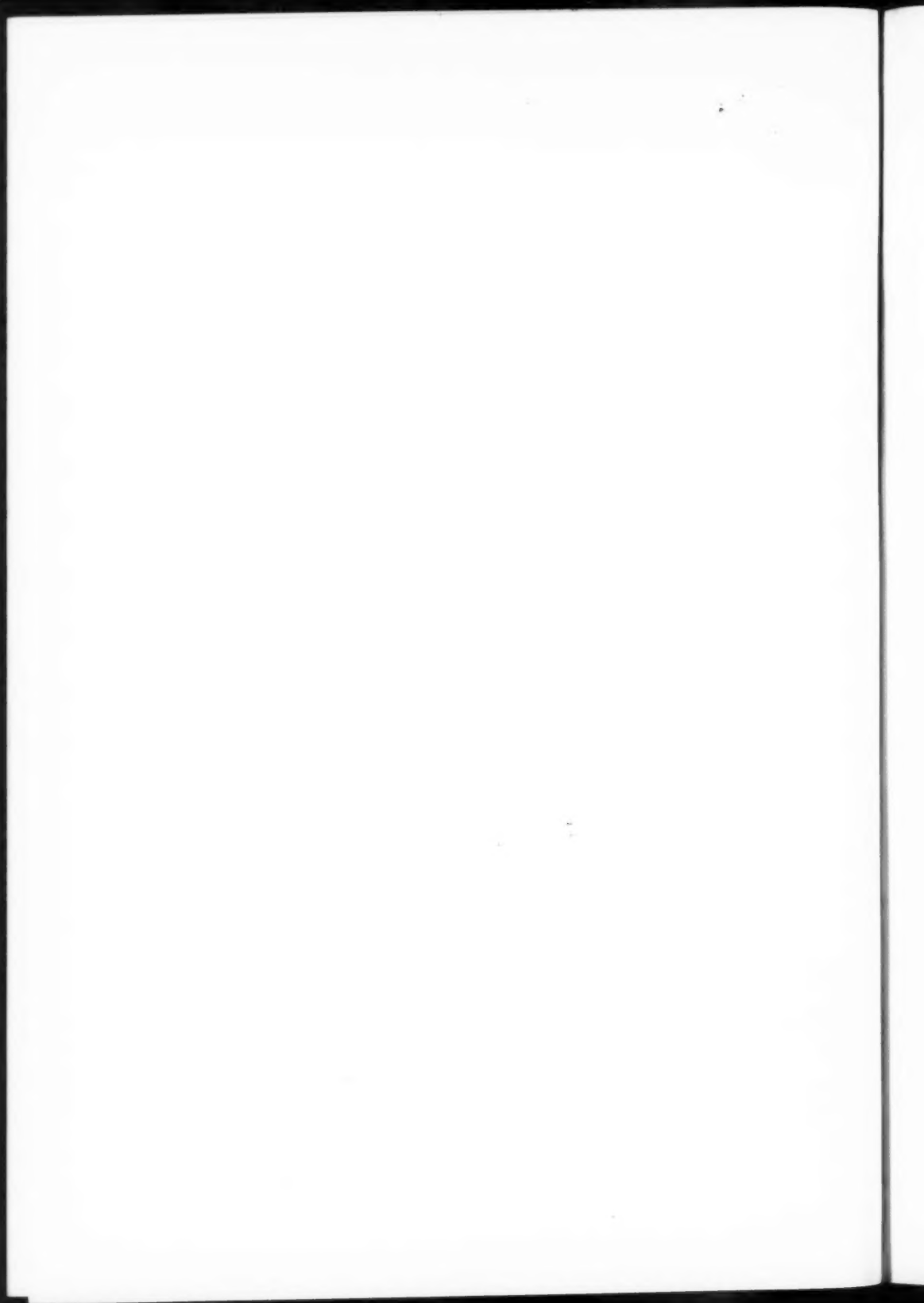
By R. R. CRUISE, F.R.C.S.

OPERATION: A large flap of conjunctiva is reflected over the cornea and trephining performed at the corneal margin. A thread of No. 2 silk suture is passed, entering the subconjunctival space 5 or 6 mm. from the margin of the flap on one side, crossing the area from which the conjunctiva has been reflected, and re-entering the subconjunctival



ERNEST CLARKE: *Unusual Arrangement of Opaque Nerve-Fibres.*





space on the opposite side to be cut off and buried 5 or 6 mm. from the point of re-entry, the proximal end also being buried. The reflected flap is sutured in position.

The object to be attained is a diffuse area of flattened boggy aqueous filtration, instead of a localized bleb of the same. Without some such device, the tendency is for the area of filtration to be limited by the area of cicatrization, and in some cases the ultimate result resembles a bubble, with a distended and thinned covering of conjunctiva, that is in danger of bursting on the slightest pretext. A point of importance is that the thread should be buried as deeply as possible in the episcleral tissue, otherwise there is a tendency to work out. The thread is left permanently. I have done the operation on my last six cases for the relief of tension and the results have all been most favourable.

The PRESIDENT considered it a very intelligent experiment, and it possessed sufficient promise and fascination for others to make trial of it, as he hoped they would. He was specially interested in the case of the man, because he sent that case on to Mr. Cruise. The eye tension was fully +3, the globe was painful, and he thought Mr. Cruise would admit him to hospital and probably enucleate the eye. But now, as members would have tested for themselves, the tension was practically normal, even if it was not slightly minus. He remembered a different form of drainage being practised many years ago. He saw Dr. De Wecker, of Paris, pass a cannula and wire through the sclerotic, leaving the gold wire in situ; but a formidable cyclitis was the almost invariable result, and not only the gold wire, but the eye had to be removed. The operation now described was one on quite different lines, and it gave promise which he hoped would be fulfilled.

### Pigmented Growth of Conjunctiva.

By F. RICHARDSON CROSS, F.R.C.S.

T. B., AGED 36; seen on February 7, 1912. R.V.  $\frac{6}{9}$ , corrected =  $\frac{6}{7}$ . L.V.  $\frac{6}{18}$ , corrected =  $\frac{6}{9}$ . Brownish thickening of conjunctiva on inner side of left eyeball, slightly overlapping two-fifths of the edge of the circumference of the corneal margin to an extent over it of about  $1\frac{1}{2}$  mm. The growth measures  $1\frac{1}{2}$  cm. vertically and  $1\frac{1}{2}$  cm. horizontally. The swelling passes in a triangular shape, with its apex at the caruncle, which is not involved. The growth is separated from the corneal tissue by an arcus senilis. (1) A small spot was seen at birth. (2) As a boy there was a dark mark and swollen area

around it about half as large as now. (3) It then seemed to stop growing. (4) When aged about 24 some hot molten lead burnt the eye and exaggerated the swelling, and it seems to have got larger since, but slowly. There appears to be general hyperplasia of the tissue of the conjunctiva in the affected area with several dark pigment markings, one of which may involve the sclerotic; but the growth is mainly conjunctival and free from the sclera.

#### DISCUSSION.

The PRESIDENT remarked that the case was possibly of serious gravity. If it were under his own care he would be inclined to remove a small portion of tissue, to submit to microscopical examination; and if it proved to be melanotic, he would remove the growth, and freely apply the galvano-cautery afterwards.

Mr. LESLIE PATON said that five or six years ago he saw a man whose palpebral conjunctiva was so pigmented as to suggest argyrosis; there were a number of plaques of pigment in the ocular conjunctiva, which, however, did not invade the sclera, though they appeared to have been present for a considerable time. About three months ago this same man became an in-patient at Queen Square. He then showed pronounced mental symptoms pointing to involvement of the frontal lobe, and he had complete immobility of the pigmented eye. He died a fortnight ago after operation. A full post-mortem examination was not allowed; but the tumour involved the whole back of the orbit, sphenoidal fissure, frontal lobe, and the tip of the temporo-sphenoidal lobe. It was a very vascular melanotic sarcoma. With this case in his mind, he therefore strongly recommended, in the case now shown, removal of the eye and the tissue freely rather than any merely local treatment.

Mr. J. B. LAWFORD said he had seen two or three cases somewhat similar, but not one so young as this man, or with such a long history. He thought it possible this had been originally a naevoid condition, and that during recent years it had become the seat of a melanotic deposit, and was now assuming a malignant character. Many years ago he showed, before the Ophthalmological Society, a woman who had a slight melanotic growth in the conjunctiva, which recurred frequently after removal, the orbit ultimately being exenterated. Death took place some years later from some internal trouble, the nature of which he could not learn. In the present case, short of radical operative measures, he would be inclined to use radium, at all events tentatively. He did not counsel any partial operation; no operation short of removal of the eyeball and contiguous tissues should be contemplated.

## Section of Ophthalmology.

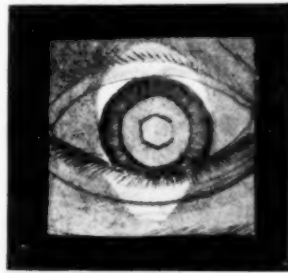
June 4, 1913.

Sir ANDERSON CRITCHETT, Bt., C.V.O., President of the Section,  
in the Chair.

### An Uncommon Case of Cataract in a Child.

By J. COLE MARSHALL, F.R.C.S.

S. B., AGED 10, attended the L.C.C. Clinic at Moorfields Hospital complaining of defective vision. Right eye: V. =  $\frac{6}{60}$ , cum -2D. sph.  $\odot$  +2.5D. cyl., ax.  $60^\circ \swarrow$  =  $\frac{6}{18}$ . Left eye: V. =  $\frac{6}{6}$ , cum +1D. sph.  $\odot$  +1.5D. cyl., ax.  $150^\circ \searrow$  =  $\frac{6}{6}$ .



Uncommon cataract in a child.

On examination one finds a symmetrically placed cataract in each eye. The opacity is hexagonal in shape, situated about the middle of the lens. The inner side of the hexagon, in each eye, is practically absent; two or three sides of each figure are much denser and more defined. The centre of the opacity is denser than the surrounding lens matter, but the retinal vessels can be seen plainly through it. The boy

has none of the usual accompaniments of lamellar cataracts, such as defects in the enamel of the teeth, neither is there any history of cataract in the family.

I am indebted to Mr. Parsons for permission to show this case.

### Melanotic Growth of the Iris.

By N. BISHOP HARMAN, F.R.C.S.

THE patient is a married woman, aged 32. She has had a healthy life until recently, when she had neurasthenia, for which she is now in a convalescent home. She has been married twelve years, and has four healthy children aged 11, 8, 5 and 2. The recent headaches suggested the examination of the eyes, and it was then that the condition of the iris was noticed. She herself was quite unaware of any change in the eye.

At the root of the iris of the left eye is a small brown lump about the size of a millet seed, and situated at the position of eight on the clock face. Its base conforms to the course of the root of the iris, the other edge projects towards the pupil in a crescent of 2-mm. radius. Its surface is raised so that it partly fills the receding angle, but does not block it. The iris is brownish-green at the root and a clearer, richer brown around the pupil, so that the lump shows up as a darker brown spot. In the ordinary state of the pupil the opening is a perfect circle, but there is a deep crease in the iris on the pupillary side of the lump as though the mass pushed the iris inwards. When the pupil is dilated with a mydriatic the dilatation is incomplete and leaves a flattened edge in the immediate region of the mass.

Examined with the corneal microscope the mass is seen to be richly pigmented and finely roughened all over; no vessels are seen. There are a few spots of grey keratitis punctata of moderate size and a good many of extremely minute size. There is a suggestion of fine dust in the vitreous in the region of the mass, but no sign of a bulge on the inner surface of the iris can be made out. Transillumination gives no help. There is no abnormal condition of the fundus. At the limbus immediately over against the mass there is a cluster of dilated minute episcleral vessels, the limbus is normal elsewhere. The right eye is normal. Vision: Right eye— $\frac{5}{5}$  partly, cum +0.25D. cyl., ax. 60° D.O. =  $\frac{5}{5}$ ; left eye— $\frac{5}{5}$ , refraction as right, not improved by glass.

The diagnosis has been put down as "melanotic growth," and this is intended to imply a malignant growth, probably growing through from the ciliary body. Evidences of inflammation, keratitis punctata and possible dust opacities in the vitreous are not usually met with in melanotic sarcomata, but their presence does not in my opinion invalidate that diagnosis. I know of no inflammatory growth that takes the character that this particular growth presents.

The treatment presents difficulties. Granting the correctness of the diagnosis, the sooner the patient gets rid of this eye the better. But no one will readily be parted from an eye that has  $\frac{6}{9}$  vision, because of a little brown spot the presence of which was not known until it was pointed out. The possibility of removing the growth by an iridectomy does not present any favourable prospects to my judgment. It involves the root of the iris and it probably involves the ciliary body, at any rate there is evidence of irritation of the latter. Excision at an early date appears the only safe treatment.

#### DISCUSSION.

Mr. TREACHER COLLINS referred to a case in which there were scattered nodules in the iris of a brown colour, and it was a question whether at first it was not simply a melanoma, and took on malignant characters later. He thought that probably the primary seat of the growth now shown was the ciliary body, the tumour extending forwards through the base of the iris into the anterior chamber. He had seen one other case of pigmented growth of the iris, and showed it before the Ophthalmological Society; it was illustrated in one of the volumes of its *Transactions*.<sup>1</sup> That growth commenced midway between the pupillary and the ciliary margin of the iris, and the patient also had a cataract. He managed to do an extraction of the cataract and at the same time remove the piece of iris containing the growth. He kept the case under observation for some time, but there was no recurrence. The microscopical characters seemed to indicate that it was a simple melanoma rather than sarcoma of the iris, though it was very difficult to differentiate between the two conditions. There was a possibility that the case now shown by Mr. Harman might be one of cyst of the ciliary body, due to agglutination of the ciliary processes, as in a case Mr. Coats had described.

Mr. G. COATS said he had not seen the case mentioned by Mr. Collins before the eye was excised, but the presence of a growing pigmented swelling in the periphery of the iris necessarily led to a diagnosis of sarcoma, and to the excision of the eye. In fact, however, the tumour was not a sarcoma but a cyst associated with the condition known as "epithelial hyperplasia

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of the ciliary processes." Apparently the ciliary processes had become agglutinated, and the proliferating unpigmented epithelium, thus imprisoned, drove the pigmented epithelium before it into the ciliary body and root of the iris, where it formed a visible tumour. As to the present case he would express no definite opinion. He was told that when the pupil was dilated the sector corresponding with the growth was flattened. This seemed to be in favour of sarcoma. On the other hand, the presence of unpigmented keratitis punctata was very unusual in tumour cases, and the cyclitis of which it was a sign might be a cause of agglutination of the ciliary processes.

### **Case of Complete Detachment of the Retina followed by Iritis ; Spontaneous Replacement Three Months later.**

By N. BISHOP HARMAN, F.R.C.S.

Miss L. S. G., aged 59, a cook in a good position. Known to have been shortsighted in school days. Was examined by different ophthalmic surgeons when aged 34, 47, and 58; the glasses ordered were mostly refused as they disturbed her sense of proportion. Since the last examination (by Dr. Halstead, of Ramsgate<sup>1</sup>) she had worn glasses until the failure of the eye. Health generally good, stout but active; after the detachment she felt confused in her head. Teeth in horrible condition, very septic. Occasionally has rheumatic pains in her feet. Urine normal.

February 9, 1913: Left a hot fire and went out into the cold; after ten minutes walk all at once something seemed to drop over the right eye and the sight went black. She saw Dr. Halstead four days later, who found a detachment of the retina. She came to me on March 5. The whole of the retina was detached in large loose billows; six were counted and sketched. Fundus colour could be seen centrally and the outer edge of the disk descried. There was central perception of light only. There were no vitreous opacities, the iris and lens were healthy. Left eye: Vision, cum -9D. sph. -1D. cyl., ax. 0° =  $\frac{9}{14}$ . Vitreous healthy, fundus second degree of peripapillary stretching. She was sent back with suggestions for treatment; the possibility of operative treatment was mentioned to her but rejected.

April 25, seen again: She said she was kept in bed as directed

<sup>1</sup> Dr. Halstead writes: "Miss G., seen autumn, 1912, R.V. cum -16D. sph.  $\frac{9}{14}$ . L.V. cum -9D.  $\frac{9}{14}$ . Did not like glasses, as things seemed to move. February, 1913: Detachment was beginning in the upper part. She said she was unable to lie up."



for a fortnight. After four days she saw things with the eye, but they were one-sided, later they got straight. But the eye felt hot and painful. Indigestion and feelings of sickness came on from lying in bed, so she got up, and the eye at once went dark again. She next went to a London Eye Hospital,<sup>1</sup> where she was put to bed for another fourteen days. Operation was proposed, but refused by her, and she left.

On examination at this date, the retina was completely detached. There was also ciliary injection, and the iris was adherent to the lens for three-fourths its circumference, the upper part (from IX to II on the clock face) was free and dilated well to atropine. No vitreous opacities, no keratitis punctata. I suggested to her doctor it was no use putting her to bed again, but to treat the iritis with atropine and fomentations, and attend to her mouth and the indigestion.

May 24: She presented herself again and said her eye was well. The ciliary injection was gone, the iris was quiet though adherent to the lens, except for the part named above. The fundus view was clear and there was no trace of a detachment. There were a very few dust-like opacities in the vitreous. In the macular region were a couple of hard white atrophic spots of small size and some dirty pigmentation; above and to the nasal side of the disk were fine interlacing black lines, just such as are seen when paper is badly pasted on to the wall. Retinoscopy: -10D. sph., -2D. cyl., ax. 30° D.O.; vision with this  $\frac{6}{36}$  one letter, but "things quivered." Projection perfect. Left vision with previous correction  $\frac{6}{12}$  partly.

June 3 and 17: Same state.

The probability is that the whole condition was inflammatory and that with the subsidence of the process the fluid behind the retina was absorbed. If this be so prognosis is good.

#### DISCUSSION.

Mr. GOUDIE mentioned the case of a man who attended the Glasgow Eye Infirmary, in whom detachment of the retina was diagnosed. About three months later the retina was found to have become re-attached. Two months later still it was again detached, and later became attached. There was fair vision, and no iritis. No operation was performed.

<sup>1</sup> Sir W. J. Collins, under whose care she was admitted in the Royal Eye Hospital, sends the house surgeon's notes: "In hospital from March 29 to April 13, 1913, with detachment of the right retina. There was no record of any iritis while she was with us, nor when she left at her own wish. Operation was spoken of, but not advised; patient strongly opposed it."

## 110 Harman: *Case of Complete Detachment of Retina*

Mr. RAYNER BATTEN said he once had a patient with very high myopia and with detachment in one eye. She then had detachment in the other eye and became blind for a year or two and had to be led about. At the end of that time she returned saying she saw a glimmer of light. She was put under iodide treatment and gradually the sight returned. She accepted her lenses again, and saw her way about. He believed her vision was  $\frac{6}{34}$ , and that she was able to read large print. She married a blind man.

Mr. HERBERT PARSONS said members were inclined to be sceptical about recovery from detachment; he had himself been so until he came across a case in which it occurred. One day when he was absent from Moorfields Hospital, a case with detachment of retina came to his clinic and was seen by Mr. Coats. The following week he (Mr. Parsons) saw the case and confirmed the view that there was detachment, and transilluminated it. The patient was admitted to hospital, but the house surgeons never succeeded in seeing the detachment, nor did anyone else. There were no streaks or anything left to show there had been detachment. He remained well for about two years, having been seen periodically in the interval, but at the end of two years he came saying the eye had gone wrong again. The retina was found to be detached again, and has remained so in spite of treatment.

Mr. MACNAB said that some years ago at the Heidelberg Conference he saw seven or eight cases of detachment of retina from Professor Deutschman's clinic; no evidence of detachment could then be found. There were places to be seen where the surgeon had cut through with the knife, and most positive evidence was given of the previous detachment. Some of them were very extensive cases, others were slight. In all these cases there had been operative measures. He had himself recently had two cases of detachment, one in a myope of 18D., who had been seen by a member of the Section. That patient had had detachment in both eyes. He had been put to bed and kept under treatment. Later there was no detachment to be seen even after the patient had been up and going about for three weeks. In the other case there had been iridocyclitis, which he believed to be due to tuberculosis of the eye. There was much vitreous opacity and a very large detachment. The eye was very soft, the cornea being dull and crinkled. Vision was bare perception of light; it required a strong light to get a reaction. He gave tuberculin and a vaccine made from the coli bacilli in the intestine for three or four months. The tension had now been normal three months. Fingers could now be counted at 5 or 6 metres. Detachment could not now be diagnosed. Neither of these two cases had been operated upon.

Mr. A. W. ORMOND referred to the case of a patient who came to see him with high myopia, and had been treated with glasses. A short time afterwards she came again stating that she had sudden failure of vision in one eye. There was obvious detachment on the outer side of the retina, which had happened two or three days before. He examined the fields, took her into

hospital and did sclero-puncture. Within four days that detachment had entirely disappeared. He had seen her a number of times since, and the attachment was still absolute, and the scar of the incision in the sclera and choroid could still be seen. Vision was  $\frac{6}{35}$ .

Mr. LESLIE PATON reminded the meeting that the case shown by Mr. Harman was one of spontaneous cure, whereas most of the cases spoken of were cures after operation. One case he showed at the old Society had had detachment in one eye for thirty-five years and in the other for eighteen months. He operated on the more recently detached retina in August, 1907, at which date vision was  $\frac{3}{60}$ , the nasal field being lost. A fortnight ago, nearly six years after the operation, he saw the patient. Vision was  $\frac{6}{6}$ , the field was full, and the patient had been following his occupation of head gamekeeper continuously since the autumn of 1907. Another case was that of a lady who had high myopia, 15D. Her vision before the detachment was  $\frac{1}{18}$  in right eye. She had had complete detachment in the left eye in 1892 and that eye was quite blind. The detachment in the right eye occurred early in 1907. On treating the detachment at one quadrant the retina became detached at the opposite pole, and he operated a second time at this quadrant. In June, 1912, five years after operation, her vision with full correction was better than it had been before the operation—namely,  $\frac{6}{6}$ . He had seen a case similar to Mr. Harman's in a girl with about 5½D. myopia, and a large detachment below, the whole lower half of the retina being detached. She was kept on her back and treated with mercury and iodide, and in three months the detachment went back, and there remained only a curious distribution of retinal pigment, very like that seen in retinitis pigmentosa. There had been no recurrence in five years. In another case there was a curious history of a man who was thrown out of a railway wagon and scraped along the embankment. He had a detachment, but did not know he had anything in his eye. X-rays revealed a foreign body, and under the idea it might be metallic a magnet was applied, and it was extracted. That detachment went back absolutely, and had remained so. He had recently been looking up some of his cases of detachment and in at least seven there was definite improvement, not only in the fields of vision, but, what counted more with the patient, in visual acuity, and in at least four cases the improvement was so great as to amount to practically restoration of normal visual acuity with no recurrence after periods of from four to six years.

Mr. NETTLESHIP suggested it might be worth while to set apart an evening to the subject at some future date, and he shared Mr. Parsons's view that members had been too sceptical about such recoveries; he had himself been so. He was sure he had in his case books a few instances in which the evidence of detachment was good, and in which recovery was also good. Most others of extensive experience must have had similar cases.

### Nystagmus on Covering One Eye.

By J. F. CUNNINGHAM, F.R.C.S.

F. B., MALE, aged 18. Seen at Moorfields Hospital, May, 1913, under the care of Mr. Lawford. Patient is a clerk, wearing right +3.5 sph., left +4.0 sph. With these right vision =  $\frac{6}{60}$  10J., left vision =  $\frac{6}{36}$  10J. Binocularly, with correction  $\frac{6}{60}$  and 1J., will not take a + sphere added. On covering either eye marked lateral nystagmus is noticed, which ceases as soon as binocular vision is allowed. When fixing with the left eye the right eye deviates upwards and slightly outwards. Patient says he had nystagmus when he was aged 4 and that it was worse then. There is no family history of nystagmus. He has dark hair and blue irides.

### On Multiple Vision with a Single Eye, technically known as Monocular Diplopia or Polyopia.

By A. M. WORTHINGTON, C.B., F.R.S.

THE main object of this communication is to produce direct experimental evidence that obscurities in the field of view, such as arise from opacities or irregularities of structure at or very near the front surface of the lens of the eye, are alone sufficient to account for all the main features of monocular polyopia as perceived by normal eyes, as well as for the peculiarities of the entoptic picture obtained by vision through a pinhole.

That much, if not most, polyopia is due to such irregularities or opacities was clearly stated in 1853 by Ruete, who rightly associates the phenomenon with the features of the entoptic picture, perceived even by healthy eyes, and already accounted for by Listing in 1845. This opinion of the origin of normal polyopia seems to have been lost sight of by later writers and has even recently been denied, partly, perhaps, because there exists another cause of polyopia in a certain combination of spherical and cylindrical aberration which is independent of such obscurations. Meanwhile new phenomena of polyopia have

been discovered which, at first sight, seem to have little connexion with any previously noticed, and the subject has become somewhat confused through the expression of contradictory opinions. Although, as one without qualification in physiology or anatomy, I should have preferred simply to record my own purely physical observations, yet I have thought that it might help to disentangle the subject and to save the time of others, if I led up to them by a brief summary of the phenomena to be explained and the views already expressed about them.

Anyone making use of only one eye will realize, if he is sufficiently attentive, that he sees multiple images of the outline of any object that is out of focus, especially when the object is a very bright one seen against a dark background, or dark against a light background. Thus an eye which cannot focus on the crescent moon, through being either short-sighted or astigmatic, or purposely prevented from focusing on it by means of a weak convex lens, will generally see two or more comparatively well defined images of the crescent which may differ considerably in brightness. Or, again, if anyone looks with one eye (focused for distant vision) towards a uniform bright background, such as the sky or the translucent shade of a lighted lamp, and then holds in front of this—at a distance of, say, 10 to 25 cm. from the eye—the edge of an opaque card or knife-blade with its plane perpendicular to the line of sight, he will generally observe not that the edge appears merely blurred as one might expect from its being out of focus, but that the transition from dark to light takes place by well-defined steps, which mark the overlapping of a succession of well-defined images of the edge. These multiple parallel rulings at the edge of the knife-blade or card often appear most numerous or most distinct at some definite inclination of the edge, which may be found by turning the card very slowly about the axis of vision and carefully watching, always taking care to keep the accommodation relaxed. It will often be found, if the edge be subsequently held at right angles to the position in which the multiple rulings are best seen, that they then disappear, so that for this position the out-of-focus edge does look merely blurred. No two eyes, even when they belong to the same individual, appear to be quite the same in respect either of the separation of the “steps” or of the manner in which these change as the inclination of the edge is altered, or in the facility with which they show the phenomenon. The fringes seen round the outlines of the finger and thumb when held nearly touching\* and too close to the eye to be in focus, are examples of the

same phenomenon familiar to most of us from childhood. Another illustration is obtained when, with a convex lens (6 or 8d.) held close to the eye, we look at a not too distant mast or telegraph post that stands out dark against a bright sky and see not one blurred mast but perhaps three or four, not equally separated nor equally dark.

The phenomena so far mentioned are easily observed, and have been long known. They were studied by Fliedener in 1852,<sup>1</sup> and were referred to by Donders in 1864,<sup>2</sup> and by Helmholtz.<sup>3</sup> Each of these latter writers dwells on their connexion with the fact that a single point of light on a dark background (or a small dark spot on a bright ground), if viewed by one eye out of focus, is generally seen as a multiple, more or less irregular, star. Consequently, as Helmholtz points out, if every bright point such as A, fig. 1, is seen as a quadruple

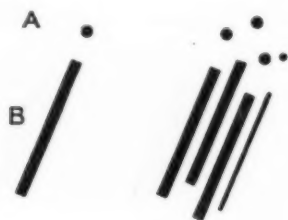


FIG. 1.

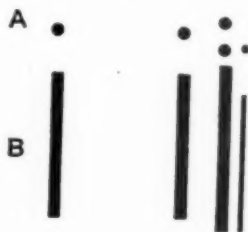


FIG. 2.

point, then the image of a bright line, B, which passes through A, will in general be a quadruple image. But if the line B were in the position of fig. 2, then two images would overlap to form a single brighter image, and the eye would then only see three images.

The list of phenomena to be explained received an important extension in 1899 at the hands of the late Mr. Shelford Bidwell, F.R.S.,<sup>4</sup> who, in February, 1899, called attention to the fact that under suitable conditions a normal healthy eye sees not merely a few—say six or eight—but hundreds of images of a single fine line, and as an illustration of further facts to be accounted for he gives a figure (closely

<sup>1</sup> *Ann. d. Phys. u. Chem.*, Leipz., 1852, xxv, pp. 321-60.

<sup>2</sup> "Accommodation and Refraction of the Eye," *New Sydenham Soc.*, Sect. 40, p. 543.

<sup>3</sup> "Physiologische Optik," Leipz., 1867, Sect. 14, p. 137, *et seq.*

<sup>4</sup> *Proc. Roy. Soc.*, 1899, lxiv, p. 241.

resembling fig. 3) which he describes as a good imitation of the appearance presented by a single horse-shoe filament of an incandescent electric lamp as seen from a distance of a few feet through a lens, concave or convex, of about 6 in. focal length, screened by a coloured glass. The number of images discernible was apparently few when the observer was near the lamp, and greatly increased as he receded from it or moved the lens farther from his eye.

Incandescent lamps with a single horseshoe filament are not now easily obtained, but I find that Bidwell's phenomenon is easily imitated by making a fine horseshoe-like cut, about 0.5 mm. wide and 4 or 5 cm. high, in a thin black card, which can be mounted on a lantern-slide covering glass and placed in front of a uniformly illuminated lamp shade. The observer, then placing his eye near it, focuses it with a convex lens



FIG. 3.

of 8 or 10D. held close to the eye; keeping the lens to his eye he then retires slowly—the curved part of the horseshoe soon looks like a ball of, first, coarse string, then fine string, and finally like a tangle of the finest silk. The phenomenon is very striking and beautiful and I recommend anyone who has not seen it to make the experiment. If the horseshoe filament is wider, then the number of images into which it splits up at a given distance is fewer, for reasons which will appear in the sequel. Thus, with a slit 2 mm. in width we may get, say, only five or six images in place of twenty or thirty. By using a strong lens Mr. Bidwell was led to estimate the maximum number of images he could see at nearly 500.<sup>1</sup>

I propose to distinguish this phenomenon of great multiplication by

<sup>1</sup> Vide Shelford Bidwell, "Curiosities of Light and Sight," Lond., 1899, p. 128.



the name of "myriopia" as opposed to the small multiplication or "oligopia" recognized by earlier observers, and shall explain in the sequel how the transition from the one to the other is brought about. It may be doubted whether this myriopia could have been discovered before the construction of the fine filament of the electric lamp, for none but a very fine filament or fine slit will reveal it, and with a fine slit the phenomenon would probably have been wrongly ascribed to diffraction.

It remains to mention a particular form of monocular diplopia (not polyopia) pointed out by Dr. F. H. Verhoeff, of Baltimore, in 1900,<sup>1</sup> which he describes as "occurring in many cases of astigmatism" (combined with hypermetropia) "or which may be brought out in the case of most normal eyes by placing concave cylindrical lenses before them." The phenomenon observed and explained by Verhoeff was the *duplication* of points, lines, and small test type. He does not seem to have observed that under special conditions, to which I shall allude later, a triplication may be reached.

In all cases the duplication or multiplication of images referred to in this brief summary disappears when the eye is accurately focused on point line or object. Verhoeff's diplopia is limited to the condition he describes, but Bidwell's myriopia is, I believe, seen by all, and as regards the earlier known polyopia, Dr. George Bull, in his paper on the "Visual Effects of Refractive Error,"<sup>2</sup> says that he has satisfied himself that "in all eyes and in every case of refractive error, including the common cases of myopia and hypermetropia, the many varieties of astigmatic vision, and the case of objects slightly outside the punctum remotum or the punctum proximum, there is found the phenomenon of monocular diplopia"—which with Bull stands for polyopia—"it is the common law of all cases where from whatever cause the object is somewhat out of focus" (p. 204, *ibid.*).

Inquiry that I have made among practising ophthalmologists in this country seems to indicate that the causes of the phenomena are regarded as still somewhat obscure and perplexed, and also, perhaps, as not of pathological importance, since the defect disappears with the choice of the right lens for correcting the refractive error; and most of my informants seem to have contented themselves with the view expressed by Donders, who asserts (*loc. cit.*, p. 546) that the polyopia arises from the fact that each of the more or less regular sectors of which the eye

<sup>1</sup> *Arch. of Ophthal.*, New York, 1900, xxix, pp. 565-72.

<sup>2</sup> *Trans. Ophthal. Soc. of U.K.*, 1896, xvi, p. 200.

is structurally built up forms a separate image, and that these separate images are usually neither perfectly free from astigmatism nor accurately superposed, nor are they even all formed exactly on the same axis. This explanation, though it would account for the formation of an irregular "star" or group of images in the neighbourhood of the focus, appears to me entirely to fail to cover the fact that even widely separated images of an object seen out of focus are at once accurately superposed when, by means of a suitable lens (cylindro-spherical if necessary) the error is corrected. If the sectors acted independently and in disagreement in the manner suggested, then a single lens would not prevent them from continuing to do so; the disagreement would remain and accurate focusing would be impossible. Bidwell's myriopia would obviously remain unaccounted for by Donders's explanation, to which also, it is worth noting, Helmholtz in the first edition of the "Physiological Optics" gives no definite support, though in a Supplement on p. 172 of vol. i of the 1909 edition we find polyopia monocularis parenthetically attributed to "irregular astigmatism."

Dr. Bull has for insufficient reasons supported Donders's explanation. In the paper I have quoted he describes how he took many photographs of test types with a camera that was first accurately focused and then put out of focus by the addition of a lens, either spherical or cylindrical, and he writes (*loc. cit.*, p. 209): "It is a curious and remarkable fact that, as my photographs will show, the camera in this respect is altogether different from the eye." Then (p. 206): "The camera has little or no diplopia (*polyopia*). The blurs and deformations of test types as seen by the eye under any conditions of refractive error may be described as invariably exhibiting bands or reduplications, which cause the usual picture in some cases to seem at first sight curiously different from the photographic plate, in which anything like marked reduplication is, in my experience, exceedingly rare, and anything like what I have called the banded appearance or the systems of resolution is never to be found." He then cut up a simple lens into sectors and put them together again *out of centre*, and placing it in his camera, of course at once obtained multiple images. On the strength of this he concludes by saying that on this evidence of the camera "we may be practically satisfied that the diplopia monocularis which we have been considering may be regarded as the diplopia of the crystalline, which is, I submit, its proper name." Dr. Bull's conclusion is thus similar to that of Donders and is refuted by the same objection—the multiple images will not disappear when you focus correctly. I have myself repeated

Dr. Bull's experiment with a lens cut into three sectors, and find that this is the case, and further that when the sectors are so accurately put together that they give a single image at the focus; then there is hardly any visible discontinuity produced by the cuts when the screen is out of focus.<sup>1</sup>

This objection to Dr. Bull's conclusion was very effectively pointed out in 1900 by Verhoeff in the important paper that I have quoted and to which I would now recur. Verhoeff's explanation—and there can, I think, be no doubt of its correctness—is that we have a sufficient cause of diplopia (not polyopia) in any astigmatic, hypermetropic eye in the fact that the lens of the eye has positive spherical aberration—i.e., in the lens of the eye, as in any ordinary uncorrected spherical lens,

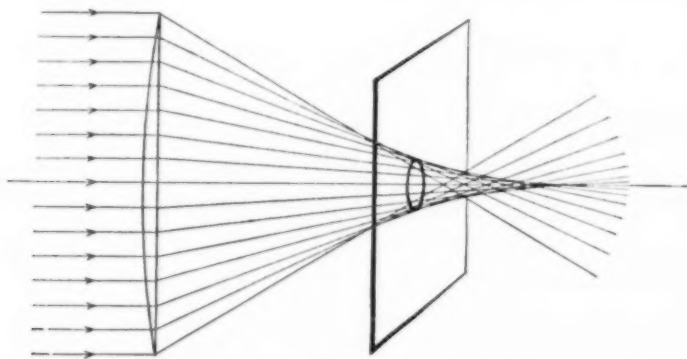


FIG. 4.

rays from the peripheral portions of the lens intersect at points nearer to the lens than rays from the more central portions (*see* fig. 4). The result is that when the receiving screen (the retina) is nearer than the focus for the central rays, then the image of a luminous point on the principal axis is represented not by a nearly uniform circular patch, as it would be if all the light were brought accurately to the same focus, but by a patch which is much brighter round the circumference, where the screen intersects the caustic curve which bounds the pencil of rays after traversing the lens. Thus the image of a small luminous spot will be a continuous uniform annulus or ring of light (fig. 5, i). But if in addition there is astigmatism—i.e., a cylindrical error—then the

<sup>1</sup> That this would be the case was anticipated by Verhoeff.

annulus becomes an ellipse, which is much brighter at each apex, so that the image is practically resolved into two distinct patches of light joined by a much fainter region (fig. 5, ii and iii). This being approximately true for every luminous point near the middle of the field, results in the duplication of the image.

Verhoeff sought to verify his explanation by taking photographs of test type by means of a large single lens of relatively short focus (11.5 cm. diameter and 26 cm. focal length) in combination with a stenopaic slit which he assumes to be equivalent to a cylindrical lens, of which, however, he could not conveniently obtain one large enough for his

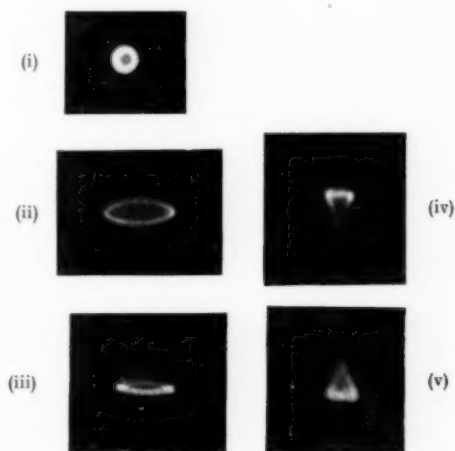


FIG. 5.

purpose, and he published a very clear photographic duplication of the smaller test letters obtained in this way. These letters were white on a black ground; with dark letters on a white ground the phenomenon, though well seen on the ground glass of the camera, did not, he says, come out so well on the plate. Verhoeff also points out that the reason Bull failed to observe the duplication was that he employed a compound camera lens in which spherical aberration was as far as possible corrected.

The experimental confirmation offered by Verhoeff would have been more convincing if he could have used a cylindrical lens to produce astigmatism instead of a narrow slit, and if he had not sought to

exaggerate the aberration by employing a lens for which the ratio of focal length to diameter was so small as 2.26—which is only about half the corresponding ratio for the eye even with a fairly wide pupil. I am therefore glad to be able to supplement the evidence by the photograph shown below<sup>1</sup> (fig. 6), which was taken with the lens of an opera-glass of diameter  $d = 4$  cm., and focal length  $f = 18$  cm., so that  $f/d = 4.5$ , in combination with a cylinder  $-0.5D$ . The object in this case was black letters on a white ground at a distance of 41 cm. from the lens. The height of the larger letters was about 16 mm., and

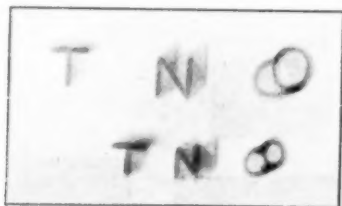


FIG. 6.

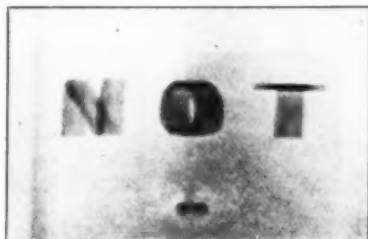


FIG. 7.

of the smaller about 11 mm. The receiving screen was 19.5 cm. from the front of the lens. The cylindrical lens was laid flat against the camera lens with the axis of the cylinder parallel to the slant stroke of the N.

<sup>1</sup>In taking photographs of this kind certain precautions are necessary. Since the object is to imitate the steady vision of the eye, slow plates should be used so that the time of exposure with full aperture is long in comparison with the time when the aperture is changing in shape during the process of closing or opening. Short exposures by means of mechanical shutters might lead to quite fallacious results. My own photographs were taken by electric light at night, the camera having already the full aperture exposed when the light was switched on. As the sequel will show, it is important to see that the camera lens is free from dust marks or other obscurities.

The upper and lower figures to the right of fig. 5 show the image of a luminous point when the axis of the cylinder was vertical, but the face of the camera and with it the optic axis of the lens was tilted respectively up or down in a vertical plane. The section of the caustic shows a cusp at which there is a concentration of light, and by this means a triplicate image is obtained. In fig. 7 there is a faint triplication obtained in this way, and the image of a dot below the O is seen to be double, with a faint cusp. By blocking out the centre of the camera lens with a circular disk so as to employ an annular aperture, along with the cylinder this triplication is much more pronounced, and by placing the object to be photographed by such a lens so that the rays struck the lens system obliquely both to the principal axis and to the plane containing the principal axis and the axis of the prism, I obtained

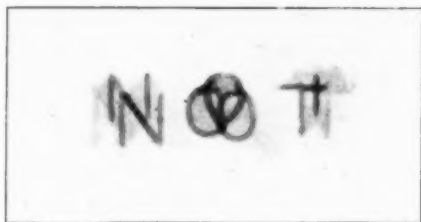


FIG. 8.

the very clear triplicate image of fig. 8, which shows what might occur with oblique vision in a living eye with a central opacity. Thus under very special conditions Verhoeff's diplopia becomes a triplopia,<sup>1</sup> but it cannot, so far as I can see, be extended beyond this, for though an algebraic analysis such as Gullstrand has conducted,<sup>2</sup> which takes

<sup>1</sup> Dr. J. W. Barrett, C.M.G., of Melbourne, in the course of his practice, had independently noticed the same phenomenon as Verhoeff, but was ignorant of Verhoeff's paper and of the cause of the diplopia. He showed me in the autumn of 1912 photographs of black letters on a white ground in which there are faint indications of more than a triple multiplication of some of the smaller letters. Prints of these photographs I have pleasure in exhibiting on his behalf, but they are unfortunately too faint for satisfactory reproduction, and Dr. Barrett was not able to recall quite sufficiently the conditions under which they were obtained. I have myself been unable to reproduce them by any device, with clean lenses. With lenses marked by even slight streaks such effects are easily obtained, for the reasons explained later in this paper.

<sup>2</sup> Helmholtz, "Physiologische Optik," 3rd ed., 1909.

account of small quantities of higher orders, may show the existence of additional cusps, yet it does not seem probable that these disturb the vision in the ordinary use of the eye, or come within the range of detection. Verhoeff's diplopia, in fact, will not account either for the multiple irregular star nor for the many banded fringes of an edge seen with direct but out-of-focus vision, nor, as Verhoeff himself points out, does it apply to a myopic eye, for if the retina lies beyond the focus for central rays the patch representing a luminous point will simply be brighter in the middle, and there is no doubling on the addition of the cylinder. I shall, however, show at the end of this paper that Verhoeff's diplopia accounts for certain other long known phenomena of out-of-focus vision.

I now come to what is undoubtedly the most important cause of polyopia—viz., the presence of local obscurities in the field of view. On this point the latest authoritative opinion that I have been able to find is that given in the "*Encyclopédie d'ophtalmologie*," 1905, iv, p. 565: "La diplopie monoculaire peut s'observer dans certaines lésions oculaires qui modifient les conditions normales de réfraction. La plus fréquente est l'opacification partielle du cristallin. Il m'a semblé qu'il s'agissait surtout de cas où de grandes opacités linéaires et radiées occupaient l'épaisseur du cristallin. Les conditions nécessaires à la production de la diplopie dans ces cas n'ont pas encore été établies expérimentalement, mais on peut admettre en se basant sur des considérations théoriques que ce n'est pas la présence de l'opacité cristallinienne seule qui peut provoquer la double image rétinienne. Il est probable qu'à l'opacification s'ajoute une modification de la réfraction cristallinienne produisant un léger effet prismatique."

I cannot conjecture what was in the mind of the writer of these words, which express an opinion so different from the clear explanation given by Ruete<sup>1</sup> in 1853, or so easily refuted by the direct experiments of which I shall now give an account.

<sup>1</sup> Ruete ("*Lehrbuch der Ophthalmologie*," Braunschweig, 1853, i, p. 135): "Double and multiple vision are caused by local obscurations of the lens and lens capsule much more frequently than by disease of the cornea. As a rule when the pupil has been enlarged by means of belladonna one can see net-shaped or star-shaped darkenings of these parts, and the majority of this class of patient whom I have examined saw many images (four, seven, and even twelve). Since they all suffered from a general dimness of vision they only saw bright objects multiplied, and these only when distant. The circumstance that when one half of the pupil was covered by a card the multiple images disappeared on that side was proof that the multiplication originated in the same way as in Scheiner's experiment." Ruete is here referring to a pathological condition, but in his admirable chapter on Entoptic Appearances (i, p. 294), he points out how universal are such local obscurations even in



Wishing to ascertain whether the polyopia of my own right eye could be imitated merely by means of obscurities on the surface of a lens, I fitted a camera with one of the achromatic lenses of an opera glass 4 cm. in diameter and 13.5 cm. in focal length. The front surface of this lens I dabbed over with plasticine clay in imitation of the obscurities that appear in my right eye when I look through a not very fine pinhole held at about 18 cm. distance, at which distance the markings seem perhaps most distinct. The result is shown in fig. 9. This first imitation is very rough and faulty and the deviation from roundness is much exaggerated, but with this lens so marked I took photographs of an imitation crescent moon cut out of opaque floor-cloth and illuminated from behind either by the light of the sky or by that of an incandescent gas-mantle, diffused by means of tissue paper laid at the back of the stencil. The diameter of the crescent was about 45 cm., and its distance from the camera about 3 metres. Fig. 10 shows the image in focus. There is here no trace of the obscurations. Fig. 11 shows distant trees in focus and the crescent correspondingly out of focus, the receiving screen being too near. Fig. 12 shows the effect when the receiving screen was too far back. In each case the lens was turned into such a position as showed the polyopia most distinctly, and it corresponds very fairly with what my eye sees, when looking at the crescent moon. Figs. 13, 14 and 15 are photographs taken with the

healthy eyes, and how indefinable the transition from the healthy to the pathological state, and in vol. ii, p. 656, he quotes from Listing's "Beitrag zur physiolog. Optik," Gottingen, 1845. After commenting on the view that "the entoptic pattern of bright streaks which is found in most healthy eyes is the picture of an umbilicate formation with seam-like and sausage-like ramifications, situated in the anterior membrane of the capsule, and originating from the separation that took place in the foetal state of this capsule from the inner side of the cornea," Listing (as quoted by Ruete) goes on to remark, "As regards the other light and dark spots and dark lines which are also found in most healthy eyes, there are many indications including the relative entoptic parallax which lead to the conclusion that the bright spots are due to transparent cells which have detached themselves from beneath the anterior capsule, and that the dark spots may be due to cataract-like darkenings of both organs (the capsule and the lens), on which account these markings are often closely related on the one hand to the previously mentioned capsule membrane, and on the other to the organic structure of the layers of the lens, while finally the dark lines may be the entopic expression of the lines of cleavage or detachment, which again are anatomically connected in the capsule with the manner of its enclosure by the cornea and with the cicatrization on its separation therefrom, and in the lens with its sector-like component parts." In connexion with this view, which, from want of anatomical knowledge, I am incompetent to criticize, should be mentioned that expressed by Professor Sigismund Exner, of Vienna, in a most instructive paper (*Archiv f. Ophthal.*, 1888, xxxiv, p. 1). He discusses the influence of minute differences of refractive index in adjacent structural parts at the surface of the lens, and shows that the dimensions of the radiant structure apparent in his own eye agree well with those of the triangular space which two adjacent lens fibres make with the lens capsule in the neighbourhood of the pole of the lens.

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same lens, very near the focus, of a small incandescent gas-mantle at a distance of about 5 metres. On the ground glass of the camera when in focus the image looked like a small, very bright point. Each of these

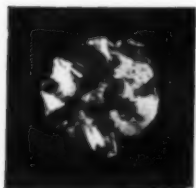


FIG. 9.

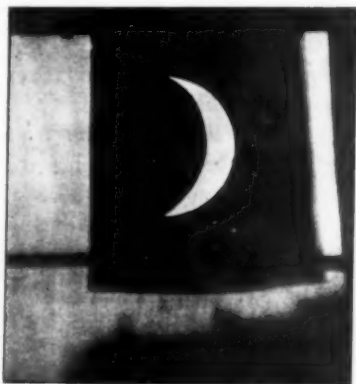


FIG. 10.



FIG. 11.

pictures will be recognized as a reproduction on a very small scale of the pattern on the lens, and they suggest the irregular, multiple, star-like images of a point that are peculiar to individual eyes.

This marked lens also gave at either side of the focus very visible

fringes parallel to an opaque straight edge seen against a bright background, but I found them much easier to see than to photograph. With the object at so considerable a distance this lens had not much spherical aberration, and the results do not differ appreciably from those obtainable with a compound camera lens in which the aberration was well corrected. I found also that it mattered very little indeed whether the front or the back surface of the lens was marked, and when using



FIG. 12.



FIG. 13.

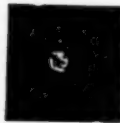


FIG. 14.



FIG. 15.

the compound lens (consisting of two widely separated achromatic doublets) and a plate glass disk marked with obscurities I found again that it mattered little whether the disk was placed just in front of the first lens, just behind the last, or between the two.

Desiring to obtain an imitation of Bidwell's myriopia, I employed the same opera-glass lens in front of which were the markings of fig. 16 made in imitation of a friend's drawing of his entoptic picture; with this I obtained the photographs (figs. 17, 18 and 19) of a narrow horseshoe-shaped slit cut in a black card in imitation of the filament

of an electric lamp and backed by a diffusing illuminated lamp shade. Fig. 17 shows the filament in focus; fig. 18 shows it out of focus (the screen being well pushed in), while fig. 19 shows the same out-of-focus view taken through a thin lantern-slide glass plate similar to that which carried the markings. This photograph shows very faint striations visible at the lower ends of the horseshoe, which are due to

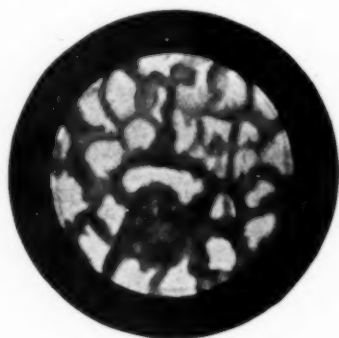


FIG. 16.



FIG. 17.



FIG. 18.



FIG. 19.

irregularities of the surface of the plate. When a piece of good plate-glass was substituted nothing of the kind could be seen.

Although with this reticulated obscuration (fig. 16) it is natural to regard the multiple images of fig. 18 as a simple illustration or repetition of Scheiner's experiment, but with many pinholes, yet when there are but a few detached markings, and these perhaps of very different opacities and relatively large clear areas, the conception of pinhole images is not so applicable, and it is more illuminating to regard the out-of-focus image in a manner which, for the purposes of the sequel, I desire to explain with reference to very simple cases.

When the image thrown on a screen by a convex lens is out of focus then the appearance presented depends not only on the shape of the object but also on the shape of the aperture of the lens and on the relation of this shape to that of the object, where by "shape of the aperture" is meant the shape as determined not only by the general contour but also by any patches of opacity that may be present. Only when the screen is in the focal plane is the image practically independent of the shape of the aperture. If, for example, the aperture is a clear circle, then (apart from spherical aberration) each point of the object

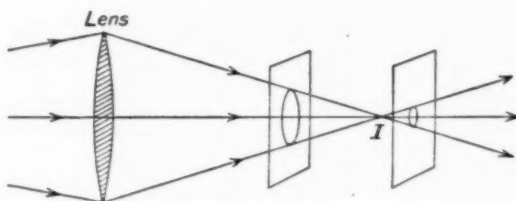


FIG. 20.



FIG. 21.



FIG. 22.

is represented by a uniform circular patch, whose diameter is proportional to the distance of the screen from the conjugate focus I (see fig. 20), and the image is made up of such overlapping circular patches. Thus the out-of-focus image of a straight luminous line will be a nearly uniform straight strip of light with well-defined edges and rounded ends (fig. 21). If the circular aperture were crossed by a diametral opaque bar (fig. 22) then the image would be made up of overlapping circular patches, each crossed by a dark bar in the same direction, and it is easy to see how, in this case, the out-of-focus image of a luminous straight line will still be a uniform (though less bright) strip, with well-defined edges, if the bar is at right angles to the line, while on the other hand if the bar is

parallel to the line we shall have two narrower bright parallel strips. Thus we shall have diplopia with the bar in one position and none with it at right angles to that position. Thus, using the same opera-glass lens as before (4 cm. in diameter) crossed by a paper strip 1.54 cm. wide, I took photographs of a fine, clear line, traced with a pencil point on a smoked glass plate backed by a luminous lamp shade. Fig. 23 shows the trace in focus; fig. 24 with the screen 1.3 cm. inside the focus; fig. 25 with it 5.5 cm. inside the focus. If with such a lens we

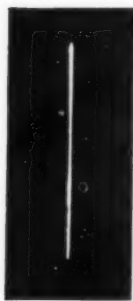


FIG. 23.



FIG. 24.



FIG. 25.



FIG. 26.



FIG. 27.

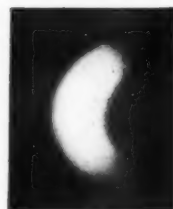


FIG. 28.

now take an out-of-focus photograph of our crescent moon, then if the bar is parallel to the upper horn, this horn which is drawn out into what approximates to a line is divided while the other is merely blurred (see fig. 26). With the bar at right angles to the line joining the horns we obtain fig. 27. The dependence of the image on the position of the bar is very striking. With the same focusing but without any bar the image was that of fig. 28. If now we cut pieces out of the bar so that it becomes a succession of patches as in fig. 29, then in the out-of-focus image of a fine bright slit, provided the bar is parallel to the slit,

we have the same diplopia as before with only a diminution in the darkness of the dividing band; but with the bar at right angles to the slit we have now the polyopia of fig. 30, each patch flinging its shadow along the image of the slit. If any of these patches were but partially opaque the corresponding shadow-band would be correspondingly weak. Next, suppose that we have a lens marked with four opaque patches, say, at the four corners of a square, as in fig. 31, we can now anticipate with considerable exactness the result of varying the inclination of the slit, if we remember that when two shadow-bands overlap they form

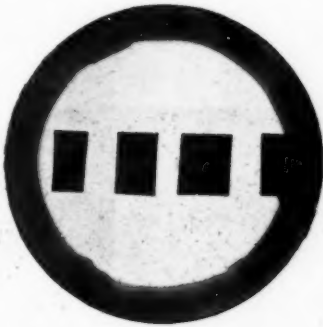


FIG. 29.

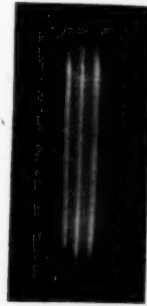


FIG. 30.



FIG. 31.

a single darker band. Thus we can pick out directions in which we shall have two, three, or four such bands, and in some positions a very slight change of inclination will make a great difference in the character of the grouping, and consequently of the resulting polyopia. The matter is well illustrated by photographs 31A, 31B, and 31C, of a slit and hole taken with a lens so marked. Fig. 31A shows the slit and hole in focus; fig. 31B shows the lens with its markings so turned as to give only two strong shadows, while in fig. 31C three shadows are thrown, one strong, two faint. We can now see that even fig. 18 may be regarded as equivalent to fig. 19 with the uniform surface scored by shadow-bands, some stronger, some weaker.



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To produce a "myriopia" we must have a multitude of shadows, and therefore of shadow-producing specks, such as are provided by the epithelial cells of the capsule of the lens. But this structure will be quite inoperative and will remain quite unrevealed unless the radiant slit is fine enough. Thus no trace of the epithelial cells is seen in the entoptic picture unless we employ a very small pinhole held within a few centimetres of the eye—or better still, the image of a small bright light, 50 or 100 yards away, viewed through a strong concave lens, say 20D., held close to the eye. For if the pinhole (or the radiant source) is too large the overlapping blur at the edge of the shadows on the retina entirely obliterates all fine detail, while again, if the pinhole be too far off the picture projected on the retina becomes too small.



FIG. 31A.

FIG. 31B.

FIG. 31C.

This is the reason that Shelford Bidwell's "myriopia" requires a very fine slit, or better still, the fine filament of an electric glow-lamp, to produce it.

In order to imitate the "myriopia," I spattered the front surface of the opera-glass lens with scrapings of black plasticine and blacklead, which on warming adhered to the glass. The appearance of the lens is shown in fig. 32. This is the "entoptic picture" obtained by means of a small hole 2 mm. in diameter at a distance of 150 cm. Fig. 33 shows the corresponding out-of-focus image of the fine filamentary horse-shoe cut in black card, whose image in focus is fig. 34. But with the wide horseshoe filament of fig. 35 and the same focusing we obtain the "oligopia" of fig. 36. The explanation of this is seen in fig. 37, which shows the entoptic picture of the same lens obtained

with a larger hole—2.9 cm. in diameter at a distance of 70 cm. It will be observed that the granulation is now automatically grouped in masses, and that there are about nine concentrations of light. The shadow-bands of fig. 36 are evidently due to such larger, opaque groupings. Fig. 37A, taken with this granulated lens and a  $-0.5D$ . cylinder with its axis parallel to the slant stroke of the N, shows Verhoeff's diplopia and opacities working together. In this case only



FIG. 32.



FIG. 33.



FIG. 34.



FIG. 35.



FIG. 36.



FIG. 37.

the largest shadow masses have asserted themselves in the picture. Without the granulation no triplopia was seen. Even in fig. 33 the number of images is not yet very great, nor are the granulations to which they are due either as numerous or as regular as those which I perceive in my own entoptic picture, or which others tell me they can see in theirs, when using a very small pinhole (say 0.1 mm. or 0.2 mm. in diameter) held close to the eye.<sup>1</sup> I therefore produced with Indian

<sup>1</sup> Under very favourable circumstances I find that from thirty-five to fifty granulations may be recognized in the diameter of the pupil.

ink on a disk of thin plate glass the close and regular mottling of fig. 38. Against this I laid a second thin disk on the face of which I had traced lightly with plasticine a *faint* six-rayed star, so as to divide the surface into six rather irregular sectors. This star is seen in the photograph, where, however, it appears far darker than the reality as seen in ordinary diffused light. Indeed, I had difficulty in photographing the marking when placed in the lantern with a ground-glass background, and the strongest impression I could get in this way is



FIG. 37A.

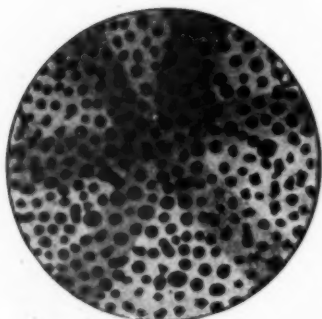


FIG. 39.

shown in fig. 39. This illustrates the great superiority of direct subjective observation in the detection of faint obstructions in the field of view of the living eye. A camera carrying this marking shows all the phenomena that I have attributed to opacities. The transition in the entoptic picture from Helmholtz's star to the fine granulation is shown in figs. 40, 41, and 42, which were taken with a compound lens free from spherical aberration. The oligopia with the wide horseshoe filament, and the myriopia with the narrow one, are shown in figs. 43 and 44. The large zigzag visible round the bend of the horseshoe

in both figures is, I find, a characteristic of eyes which see sectorial divisions in the entoptic picture.

A still closer imitation of one of Helmholtz's drawings of his entoptic "star" is shown in fig. 45, which was obtained by means of a similar faintly traced seven-rayed star, used in combination with the same

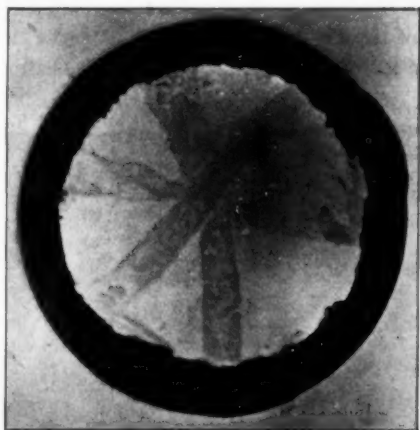


FIG. 39.



FIG. 40.

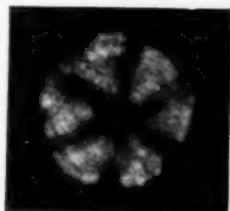


FIG. 41.

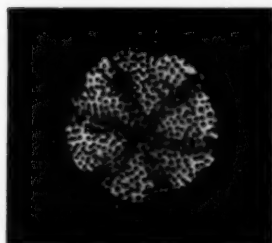


FIG. 42.

spotted disk. This time, however, the opera-glass lens (which has spherical aberration) was used, and close behind it was placed a  $-0.5D$ . cylinder, with its axis nearly vertical. The effect of this cylinder was, however, purposely somewhat reduced by giving the camera a slight horizontal obliquity. The sensitive plate was just outside the second focal line. When inside the first focal line a dark centre was shown

instead of a bright. Fig. 45 closely resembles Helmholtz's fig. c.<sup>1</sup> Since all the dark markings disappear from this photograph as also from fig. 40 when a clear lens is used, it appears to me that Dr. Gullstrand's discussion of Helmholtz's star,<sup>2</sup> which, if I understand him aright, would trace Helmholtz's pictures to aberrational errors of refraction, is wide of the mark.

I have spoken throughout of *opacities* and *obscurations* at or near the front surface of the lens as the cause of polyopia, but I do not wish by the use of these terms to imply anything more than shadow-throwing



FIG. 43.

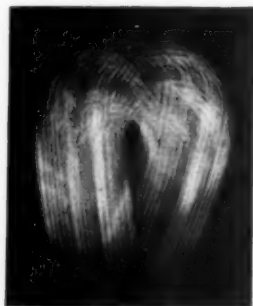


FIG. 44.

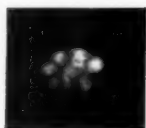


FIG. 45.

obstructions to the direct passage of the light. Minute irregularities of the surface, slight refractive differences between adjacent structural parts themselves quite transparent,<sup>3</sup> will suffice to determine such shadows without the aid of any really opaque deposit, though I imagine that this is seldom quite absent from the eyes of old persons.

To give a practical illustration of the action of purely transparent

<sup>1</sup> "Physiologische Optik," 3rd ed., i, p. 161.

<sup>2</sup> *Op. cit.*, i, p. 359.

<sup>3</sup> Vide Exner, *Archiv f. Ophthalm.*, 1888, xxxiv, p. 1.

obstruction, I poured on to the surface of a clean lantern-slide cover-glass a thin layer of a very dilute solution in chloroform and ether of Canada balsam. This, when dry, seemed perfectly clear, but showed to careful examination minute irregularities. By diffused daylight only the larger markings on this plate are observable, but when it is put close in front of the camera fitted with the opera-glass lens as objective, then, with a sufficiently small radiant, the pattern of fig. 46 is well seen, in which a general minute granulation is to be detected. With this marking was obtained the brilliant myriopia of fig. 47, besides strong oligopia and shadow fringes.

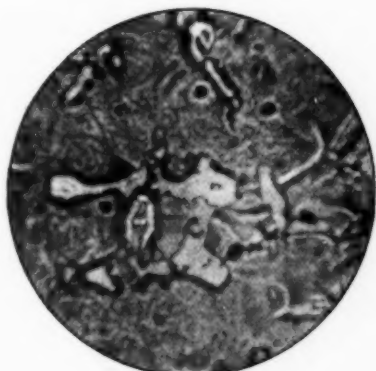


FIG. 46.

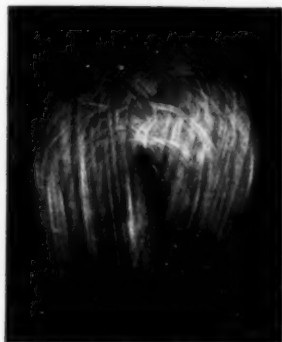


FIG. 47.

That the obstructions with which we are concerned lie very near the plane of the pupil is proved by the absence of parallax with reference to the projection of the pupillary aperture when two neighbouring pinholes are used for obtaining the entoptic picture.

I desire now to touch upon some isolated points arising out of the observations, but not essential to the previous argument:—

(1) Although the shadow-bands fringing the edge of a dark body are easily seen on the camera screen even when thrown by faint obscurations, they are not easy to photograph well enough for good reproduction unless dense opacities are used, such as would correspond rather to a pathological, or at least a senile condition of the lens. Fliedener mentions<sup>1</sup> that a very good way of bringing such bands to the notice of those who do not readily see them—e.g., round the edge of a finger

<sup>1</sup> *Ann. d. Phys. u. Chem., Leipzig*, 1852, xxv, pp. 321-460.

held up against a bright background too near for the eye to focus—is to place finger and thumb together so as nearly to touch. In this case a narrow slit is made in which shadow-bands may always be detected, and these are then seen to extend themselves into fringing stripes where the slit widens. If one of the two digits is nearer to the eye than the other the view of the second is partly obscured, and the illusion is produced of a dark protuberance rising from the more distant to meet the nearer as it approaches. These phenomena are well shown in fig. 48 (taken with the opera-glass lens and the six-rayed star, from a card stencil cut to represent the outline of thumb and finger, the right hand card being nearer to the lens than the left). The discontinuities in the shadow in fig. 48 are a sure sign of shadow-bands



FIG. 48.



FIG. 49.

and, therefore, of obstructions on the lens. Fig. 49, taken with a clear lens and the two parts of the stencil in the same plane, shows no shadow-bands. This photograph brings out very clearly the *bright* external fringe bounding each shadow. This bright fringe is easily proved to be an outcome of positive spherical aberration, for it is never seen unless the image of a point in the object is represented by an annulus on the receiving screen. Thus in fig. 49 the right-hand limb of the card stencil, from which the photograph was taken with the clear opera-glass lens, was pierced by a small hole, the image of which appears as a luminous ring whose diameter is seen to be equal to the horizontal distance of either fringe from the edge of the complete shadow. With the screen at the other side of the focus the point was represented by a patch brightest at the centre, and no fringes were seen. The curvatures of this lens are such



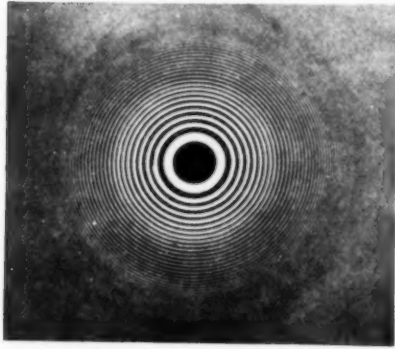


FIG. 50.

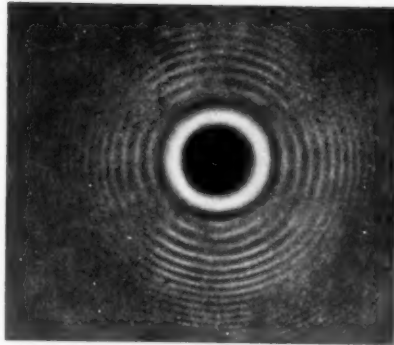


FIG. 51.

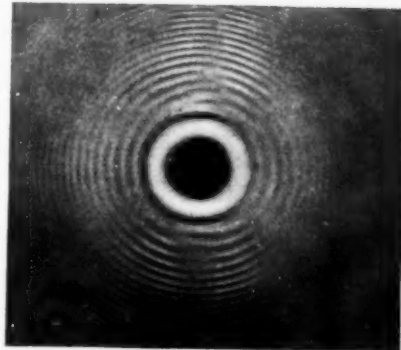


FIG. 52.

that when it is used to throw an enlarged image on to a distant screen, the annulus and the bright fringes are very well seen if the lens faces one way, but on reversing the lens the spherical aberration is corrected, the annulus becomes a uniform patch, and the fringes disappear. Experiments with other lenses, both simple and compound, showed always the same interdependence. One compound camera lens that I have shows bright fringes at both sides of the focus, but it also shows an annulus at both sides. The positive spherical aberration alone would, however, not explain why the fringe is brighter than the general field. But this appears to me to follow without difficulty from the known phenomena of diffraction, the brightness arising in fact from the *additional* illumination close to the edge that is due to light from behind the object inflected by diffraction into the peripheral parts of the lens which it would otherwise miss.



FIG. 53.

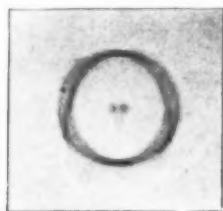


FIG. 54.



FIG. 55.

(2) On p. 163 of vol. i of the third edition of the "Physiologische Optik," Helmholtz calls attention to the radial dimnesses that are seen when looking at a pattern of fine concentric circles, and points out that where two adjacent segments of the same circle meet at a dimness they no longer fit each other, and he also describes the curious appearance of a flickering motion when the accommodation of the eye changes. It is almost inevitable that such a phenomenon should suggest the sectorial anatomy of the lens (cf. fig. 20, p. 28, op. cit.), and it was, I confess, with surprise that I found that what is apparently the same phenomenon is producible by the camera with clear lenses. Thus fig. 50 is a reproduction of a drawing of concentric circles, convenient for the purpose, copied from Woods's "Optics," p. 30. Fig. 51 shows the same figure as viewed out of focus with the clear opera-glass objective, close in front of which was placed a  $-0.5D$ . cylinder with axis horizontal. Fig. 52 shows the same thing, but with a  $+0.5D$ . cylinder. In this

figure the disagreements of the circles are more clearly seen. To analyse the phenomenon I took photographs with the same clear lens and a  $-0.5D$ . cylinder with axis vertical, first of a single ring with a dot at its centre (fig. 53) held vertically in front of the camera, but with its centre slightly below the optic axis of the objective; the result is shown in fig. 54. It will be noticed that there are six dark places with fainter gaps between, and that there is a symmetry about a vertical, but not about a horizontal, axis, as indicated by the divided cusped caustic, which represents the dot at the centre of the circle. This is the same cusped figure as was given in fig. 5, iv, p. 119, where its origin is explained. On repeating the experiment with the object just above the axis of the objective, the figure is reversed, and we have



FIG. 56.



FIG. 57.



FIG. 58.

fig. 55. Passing now to the two concentric circles, shown in focus in fig. 56 with a dot above and below, with their centre just below the axis of the camera, focusing them accurately without the cylinder, and then inserting the cylinder, we obtain fig. 57, in which the six radial dimnesses are seen nearly symmetrically disposed. A very slight alteration of focus, however, with a very careful adjustment of level, turns this into fig. 58. The adjustments for perfect symmetry, I found, were rather difficult and of a triple kind. The focus must be midway between the focal lines, and the centre of the circles exactly on the optic axis, and the plane of the circles perpendicular thereto. The equilibrium of the appearance presented by such circles to an astigmatic eye is, therefore, unstable; and the slightest motion of the eye will topple the system from the configuration implied by fig. 54 into that

of fig. 55, and the slightest change of focus will shift us from fig. 57 to fig. 58, and this instability explains the flicker. To trace the shifts in the pattern more minutely would require better apparatus than I possess.

In case anyone interested in the study of the out-of-focus image presented in this paper desires to repeat any of the experiments, I may mention that I have used in the photography "Imperial" dry "Process" plates, speed No. 12 (the slowest I could get); and that for projection on a screen before an audience the radiant objects (slits, crescents, holes, &c.) have been stencils placed in the projection lantern with a dispersive backing of very fine and transparent ground glass, carefully selected with the view of avoiding unnecessary loss of light.

### Case of Cyst of Iris.

By G. H. POOLEY, F.R.C.S.

MISS I. L. First seen by me on November 27, 1911, on account of an error of refraction and some blepharitis. On examination there was a black mass in the substance of the iris projecting backwards. It was globular in outline and projected slightly into the outer part of the pupil of the right eye when it was fully dilated by a mydriatic. The vision of both eyes was normal with a correction for a small amount of hypermetropic astigmatism. I warned the patient that this was either a cyst or a new growth and suggested that an opening should be made into it to see if it was a cyst, on the understanding that if it was solid the eye should be removed forthwith. The case was seen in consultation by Mr. Lang and Mr. Grimsdale, who confirmed my opinion.

On December 11, I noticed that the spaces in the stroma of the iris, which was a light-coloured one, were opening up and showed distension of that part of the iris immediately over the cyst. On the same day I transixed the mass with a needle and cut through part of the wall, when the cyst collapsed absolutely. Recovery was uneventful, except for a little circum-corneal injection for a few days, and she left the Home on December 16. She has been under observation until March, 1912, and there has been no return of the cyst and the sight has remained normal.

I had previously seen a similar case, also on the outer part of the iris of the right eye. In the case of Mrs. M. whom I saw first on December 9, 1910, for an error of refraction and conjunctivitis, the condition was practically similar to the one above. I advised the same treatment, and kept her under observation until the middle of June, 1911, when I noticed some opening of the spaces in the stroma and the appearance of a little black dot at the bottom of two of these spaces. There was only slight bulging of the front of the iris. I lost sight of this patient after this, and was told shortly after that she had been to London and had had her eye removed there. As far as I can understand from the general practitioner who gave the anæsthetic, no needle was put into the mass, and as this so closely resembled the other, which proved to be a cyst of the iris, I should very much like to see a section of this eye. She had also normal sight in each eye with a glass for a similar amount of hypermetropic astigmatism, and had suffered no pain.

It is interesting to note that neither of these patients had felt any pain, that the cyst was only visible as a small black mark at the periphery of the iris when the pupil was fully dilated.

*Bibliography.*—There was no adhesion of the iris and no evidence of any previous inflammation of the iris in either of these cases. The pupils dilated evenly and fully. The first case, at any rate, was probably one of the group of cysts of the retinal epithelium of the iris—i.e., between the two layers of the pigmented epithelium (*see* Parsons's "Pathology of the Eye," 1904, i, p. 318). There is a strong resemblance to the case reported by Mr. M. C. Mayou in the *Transactions of the Ophthalmological Society*, 1905, xxv, p. 86, which also affected the outer part of the right eye. Somewhat similar is the case reported by Mr. E. Clarke in the *Transactions of the Ophthalmological Society*, 1907, xxvii, p. 83, also affecting the right eye down and out, though here there was some inflammation. These cases resemble Cases 9 and 10 reported by Mr. Treacher Collins in the *Royal London Ophthalmic Hospital Reports*, 1890-93, xiii, pp. 58-61, and differ from the group of cases secondary to inflammations and adhesions of the iris, also reported by Mr. Treacher Collins in the same paper, and the case reported by Mr. Brewerton in the *Transactions of the Ophthalmological Society*, 1909, xxix, p. 143.

**Case of Corneal Ulceration associated with the Presence of  
Spirilla and Fusiform Bacilli.**

By W. G. GOUDIE, M.B., and J. R. SUTHERLAND, M.B.

M. J. T., AGED 14, an inmate of an industrial school, was admitted to the Glasgow Eye Infirmary on November 22, 1912, suffering from a profuse discharge from each eye. Regarding her previous health and her family history no details could be got. The girl was illegitimate, mentally defective, and friendless.

Her present illness commenced a fortnight before her admission to hospital, and was characterized by the sudden onset of pain in each eye and by the appearance of discharge from each conjunctival sac. The discharge appears to have been profuse and purulent from the start. No cause could be given for the occurrence of this illness. There were no cases of eye trouble in the school at the time, nor had there been any for some time previously. There was, however, an epidemic of "sore throat" in a town not far from the school, and some of the scholars who were in the habit of going to the town contracted this trouble. In the opinion of the medical men who treated those suffering in this epidemic, the condition was not diphtheritic in nature, and was not accompanied by any eye symptoms. Our patient, although she had been in close contact with these scholars, escaped infection.

Present condition (November 22, 1912): Patient is poorly developed but healthy. No signs of tuberculous or of syphilitic disease can be discovered. (A Wassermann test carried out at a later date gave a negative result.) The condition of the eyes is as follows:—

Right eye: Both eyelids are red and swollen. Slight pressure over the upper eyelid causes an escape of pus from the conjunctival sac through the palpebral fissure. Owing to swelling of the lids and blepharospasm a view of the cornea is obtained with difficulty. When exposed it is seen to be deeply ulcerated, corneal denudation having occurred at three relatively large areas to such an extent that Descemet's membrane is exposed at each of these positions as a black glistening prominence. Intact cornea is represented only as narrow strands separating these keratoceles and as a narrow ring at the peripheral margin of the cornea. In these situations it appears to be infiltrated with pus. Hypopyon and turbid aqueous humour prevent inspection of the iris and deeper structures of the eye.

Left eye: In the case of this eye less corneal ulceration has occurred. The appearance is otherwise very similar to that of the right eye. The lower half of the cornea is occupied by an ulcer, the floor of which is formed by Descemet's membrane. The upper half of the cornea is infiltrated with pus. Hypopyon and turbid aqueous humour exist as in the case of the right eye. Both tear sacs appear to be healthy, and nothing abnormal can be discovered in the condition of the nose or throat. Repeated irrigation of both sacs had the effect of reducing the discharge so that in six weeks it had almost ceased. Three months from the date of the onset of the illness both corneæ were healed, but were leucomatous to such an extent that vision was *nil*.

#### BACTERIOLOGICAL EXAMINATION.

Films were made from the discharge and stained by Gram's method, weak carbol-fuchsin being employed as a counter-stain. These films showed numerous organisms and polymorphonuclear leucocytes. Of the organisms those most striking in appearance and point of number were spirilla and fusiform bacilli. The former were long and attenuated, presented four to six large irregular curves on their bodies and lost Gram's stain. They appeared to take on the counterstain somewhat faintly. The fusiform bacilli, much shorter and stouter than the spirilla, also lost Gram's stain, but stained deeply with the carbol-fuchsin. They tapered to a point at their extremities and presented an unstained middle portion. The remaining organisms to be seen in the films included Gram-positive cocci and Gram-positive bacilli. The former were arranged mostly as diplococci. A few were lodged within the bodies of the polymorphonuclear leucocytes, but the great majority were extracellular. The Gram-positive bacilli referred to, apart from taking on Gram's stain intensely, offered no distinctive features. This state of affairs existed in the case of each eye.

Swabs were taken from patient's throat and nostrils, but in none of them were to be seen spirilla or fusiform bacilli.

By inoculating various culture media with the discharge from the eyes it was possible to isolate the Gram-positive cocci and Gram-positive bacilli described above. Repeated attempts to grow the spirilla and fusiform bacilli on media, under circumstances generally regarded as suitable for the growth of such organisms were unsuccessful. This is the more remarkable, when one considers that these organisms could be demonstrated microscopically in the pus for a period of two weeks dating from the time when the case first came under our notice.



The Gram-positive coccus which was isolated from the discharge grew readily at room temperature in all the ordinary media, producing complete liquefaction in a gelatine stab preparation in about seven days. Growth in agar was vigorous, and ultimately assumed a yellow colour which appeared about the tenth day. In tubes of broth containing separately saccharose, lactose, mannite, maltose, glycerine, an acid reaction was produced in each. Raffinose, inulin and salicin were unaffected. The same organism reduced nitrates to nitrites and clotted milk. In films made from the cultures it appeared as a typical Gram-

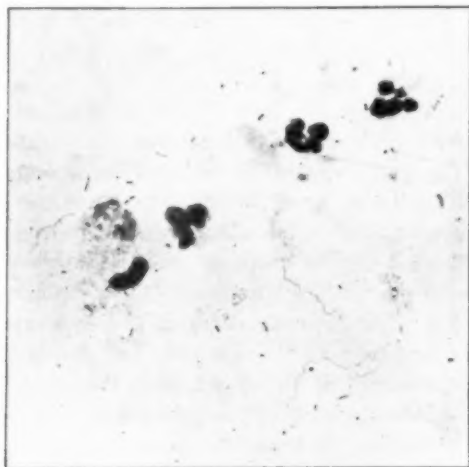


FIG. 1.

Fusiform bacillus and spirillum.

positive staphylococcus. Its staining reaction and cultural properties thus correspond to those of *Staphylococcus aureus*.

The second organism obtained in culture from the pus—namely, the bacillus—did not grow on agar or gelatine. Growth on inspissated serum appeared in the form of small white tough colonies. With the exception of its action on glucose and saccharose, both of which it fermented, this organism had no apparent effect on the sugars usually employed for the differentiation of organisms. Stained by methylene blue, Neisser's stain, and the Gordon-Pugh stain it presented a striking similarity to the *Bacillus diphtheria*, but from a consideration of its

cultural characters and from the fact that it proved non-pathogenic to a guinea-pig when injected subcutaneously, we are inclined to the view that it was the *Bacillus xerosis*.

The virulence of the staphylococcus and of the bacillus was tested on the guinea-pig's eye. The cornea of a guinea-pig was abraded by means

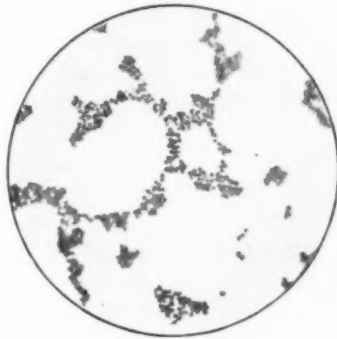


FIG. 2.  
*Staphylococcus.*

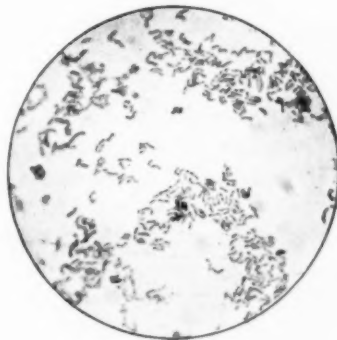


FIG. 3.  
*Bacillus xerosis.*

of a sterile needle, and an emulsion of the organism instilled into the conjunctival sac. Two guinea-pigs were employed in the tests, one for each organism, and in neither case did any sign of corneal or conjunctival inflammation result.

The actual pus from the patient's eyes was not tested in the same

manner. Whether the spirilla and fusiform bacilli acting together or separately were virulent to these tissues was not ascertained experimentally, but it seems likely from the avirulent character of the staphylococcus and *Bacillus xerosis* that the marked destructive changes which occurred in the patient's corneæ could not have been produced solely by them.

In any case, the presence of spirilla and fusiform bacilli in an inflammatory condition of the eye appears to us so uncommon as to induce us to record the preceding observations.

We are indebted to Mr. Fergus for his kindness in permitting us to publish this case.

### The Education of High Myopes.

By N. BISHOP HARMAN, F.R.C.S.

At the British Medical Association Meeting of 1910<sup>1</sup> I gave an account of an experiment that had been initiated in London for the satisfactory education of children who were suffering from myopia to such an extent that they were not suitable subjects for any ordinary educational curriculum. Since that date there has been an extension of the work on the lines then indicated, and it is thought that the publication of the lessons learned by the working out of that educational scheme may be of assistance to others.

The demand for some scheme of education suitable for children suffering from a defect of vision is a very natural one. It is bound to arise when education is made compulsory for every child by Act of Parliament. It is bound to arise because no one scheme of education will cover all cases. The curriculum of any school is designed for the greatest good of the greatest number. Misfits must suffer, either because they are incapable of taking advantage of the education provided or else because the scheme would be injurious to them if their full attendance were insisted upon. This was early recognized in the case of the blind, and special forms of education were provided for them, and in the case of elementary school children extra grants were given by the State to meet the additional cost of their special educa-

<sup>1</sup> Harman, "The Education of High Myopes," *Brit. Med. Journ.*, 1910, ii, p. 1320.

tional needs. The difficulty became acute in the case of those who had serious defect of vision, and yet were not blind, and not likely to become blind. When such cases came to the ophthalmic surgeon he very rightly objected to the attendance of these defective children at the ordinary school; it was not right to subject them to the strain involved. In the end the children either were exempt from school altogether or they were drafted into the schools for the blind and partially blind under the definition given in the Act providing for these schools. Neither of these alternatives was satisfactory. In the first case the child loafed about the streets or became the household drudge, and the more intelligent of them took their lessons from their normally sighted colleagues and read without restraint under the worst conditions; indeed, the very aim of the exemption from school was defeated. Further, it must be recognized that the denial of the communal life of the modern school was a real loss to the children, and one that was recognized by the children themselves. In the second case the admission to the blind school had its own drawbacks. The children had to associate with the blind, and do the work of the blind, yet they themselves were sighted children and for the most part not likely to become blind, certainly not in school years. The work they learned was waste of effort and utterly useless. Teaching Braille to a short-sighted child is misplaced energy of the worst kind, for the child will not read it with its fingers, but at the instant the teacher's back is turned the child bends down its head to read with its eyes bare impressions on the paper, which are vastly more difficult to see than ordinary black print. Again the labour was wasted, for no such child ever dreamed of reading the limited works of the Braille Press after leaving school; if it wished to read, it read the books of the normal children of the household. Lastly, and this is the most serious matter for the children of the working classes, the child left school with the stigma of the blind school upon it. And in these days of Employers' Liability Acts that is no light matter. When a child leaves school and applies for work it is the usual thing for the would-be employer to ask from what school the child comes, and the standard passed; the mention of blind school is sufficient to terminate the interview, for who will run the risks that the employment of the bad-sighted entails?

These things were drawn attention to at the International Congress of School Hygiene in London in 1907,<sup>1</sup> and from that arose the first

<sup>1</sup> Harman, "The Mental Characters associated with Blindness, &c.," Second International Congress of School Hygiene, 1907, p. 794.

attempt to deal with this particular problem. These myope classes of which I shall give an account are provided for elementary school children, but the methods employed are applicable to any class of child, and to the education of single children by tutors at home. There is no particular novelty in the method, it is the mere application of common-sense to the situation. Indeed, it is a return to the primitive, almost prehistoric methods of education such as must have existed amongst our woad-tinted forebears, when the wise one of the tribe taught the traditions of the fathers to the children, initiated them in the secrets of their cunning handiworks, and showed them how to make the tribal marks upon the walls of their huts and caves. There, in brief, is the scheme of the myope class, it is essentially personal, and lacking in that modern substitute for personal teaching, the book.

#### METHOD OF SELECTION OF CASES.

One afternoon each week at a certain place in London, twenty children who are reported by the hospital doctor, the school doctor, or other authority, as suffering from serious defect of vision are brought for examination. Each child is examined, note made of the state of the eyes, and such vision as may be present, and some decision arrived at as to what education is possible for each child. Some are returned to the ordinary school as capable of receiving the regular education. Others are graded for various degrees of exemption or special treatment up to the admission to the blind schools :—

- (1) Elementary school for easy treatment as regards eye work.
- (2) Elementary school for oral teaching only.
- (3) Myope class.
- (4) School for the blind and partially blind.

Many are invalided temporarily for treatment, some are transferred to country homes, but the majority fit into one or other of the four classes named above. Each case is considered on its merits, and many conditions besides eyesight influence the decision arrived at—e.g., the age of the child, whether one or both eyes are affected, the nature and degree of the affection, the possibility of amelioration or aggravation during school age, the possible effects of school attendance and work, the possible educational advantage of a change of regime, it may be both at home and at school, and lastly, in the case of the blind and partially blind, the most suitable school for the particular child in the knowledge of his or her age and capability.

Of the four groups named above one is a temporary expedient and liable to produce unsatisfactory results. It is the result of the rapidity with which suitable cases for entry to the myope classes are reported and slowness with which provision for these classes can be made. Up to the end of 1912 there had been entered on the roll of the myopes 300 children, but there was only room for 100 in the new classes, the remainder had to be accommodated in the ordinary schools but under special conditions; they were admitted for oral teaching only. Children admitted to elementary schools under such limitations are obviously in an anomalous position, and their presence must be a source of difficulty to the teachers in that they disturb the normal routine. Also they are likely to fall into a sort of backwater in the school life, a condition not favourable to their development. But despite these difficulties there is on the whole some advantage to the child, who is better off in the school than loafing at home or on the streets, and it would be quite easy to demonstrate that the children prefer it. At the lowest estimate they gain by the discipline of school life.

To make clear the nature of the defect of the eyes of these children and the limitation of the education they will receive, the matter is explained personally to the parent of the child, and a notice to the following effect is given:—

#### NOTICE REGARDING THE CARE OF THE EYES.

##### *To the Parents or Guardians of*

Your child suffers from a defect of vision that prevents him or her from joining in the ordinary work of the school. If it is impossible for you to obtain admission for the child to a special class for short-sighted children he (or she) may attend an elementary school with a view to gaining the educational advantage of school discipline and such general knowledge as can be given in the oral lessons of the classes. Reading and writing of any kind will not be allowed except blackboard work. You are particularly asked to watch your child at home, to teach games and outdoor play, and to stop all reading and writing. (In the case of a girl, sewing should be completely stopped, but knitting may be learned provided the child does it by feeling the stitches and not by looking at them.) The child should be out of doors as much as possible.

It is equally necessary that the teachers to whose care these children are committed should be clear as to the necessity for closely watching and limiting their work, and to this end a circular letter is sent to the headmaster of the school to which any such child is admitted:—

TEACHING OF CHILDREN RECOMMENDED BY THE MEDICAL OFFICER FOR  
"EASY TREATMENT AS REGARDS EYE WORK" OR "ORAL TEACHING ONLY."

*Children recommended for "Easy Treatment."*—These children usually suffer from a defect of one eye only or they have defective vision in both eyes of a moderate degree. With reasonable care school work should not cause strain of the eyes or entail the risk of exaggeration of their visual defect. These children should sit in the front row of the class, sit upright and not be allowed to stoop over any literary work allowed them. Girls must do no sewing, but may learn knitting, provided it be taught by touch and not by sight. Boys and girls should be prohibited the use of books with small print or writing of any sort other than a bold, large-lettered hand. They should not join in exercises that involve the reading or writing of masses of numerals or geometrical figures. They may read or write in large type, preferably for periods not exceeding twenty minutes without a break. They should not be allowed to stoop over their work, and if it be possible, the writing should be done free-arm fashion on a blackboard or millboard set up on the desk.

So far as school arrangements allow they should attend all the object lessons, demonstrations and oral lessons that are given in the school.

Drill, dancing, games of all kinds may be freely indulged in.

Home lessons of any sort should be prohibited.

*Children recommended for "Oral Teaching only."*—These children suffer from some serious defect of vision, such as gradually increasing short sight. When no place can be found for them in a special class they are admitted to the elementary school with a view to their gaining the educational advantage of school discipline and such general knowledge as can be given them in the oral lessons of the classes.

The use of books, pens, paper, pencils and slates of any kind and for any purpose is to be prohibited and the child should be reminded at intervals by the teacher in a friendly chat that the prohibition is for his or her own benefit, and that they must do at home what they are trained to do at school.

If the class arrangements permit they may be allowed to write or draw on the blackboard in large characters free-arm fashion.

If a girl shows aptitude for handwork she may learn knitting by touch, but not by sight. Similarly a boy may do the larger kinds of carpentry, but he must not use the rule or draw measured plans.

For the most part these children may drill and dance, but they should be warned against using gymnastic apparatus or dumb-bells, for example, in connexion with the Children's Happy Evenings Association. They should be cautious in the playground games.

But even presuming the greatest understanding and watchfulness of the parents at home, and the greatest readiness of the teachers at



school to make the necessary allowance for such abnormal units in their classes, this arrangement for the admission of myopes of high degree to elementary schools for oral teaching only is a makeshift, and only permissible with a view to its speedy abolition.

#### THE MYOPE CLASS.

The first necessity for the successful establishment and working of such a class or school is that it shall be associated with an ordinary school for normal children. The myope class must be considered and worked as an integral part of this school. The reasons for this prime necessity are three: (1) A better scheme of work can be provided by this association; (2) to establish the class as a separate unit is to run the risk of the children leaving school with a special mark upon them; (3) parents naturally object to any suggestion of their children being marked out as belonging to a particular class of defective child, even though it may be for their good, and for this reason the attempt which has been made to copy the London experiment in the provinces by establishing myope classes within the existing blind schools has proved a failure. It cannot be too definitely insisted upon that the only possible means of making these classes a success is by associating them, both in their practical working and in their classification with the ordinary schools; for that reason in London they are always spoken of as "classes," and never as "schools." The scheme of work laid down for these classes is as follows:—

(1) Oral teaching with the normal children for such subjects as can be taught orally.

(2) Literary work such as is necessary for the knowledge of the ordinary means of communication to be learned without books, pens, or paper, but by the use of blackboards and chalk, the writing to be done free-arm fashion.

(3) A very full use of every sort of handicraft that will develop attention, method, and skill, with the minimum use of the eyes.

After four years' experience with the experimental class and the extended observation of the work in two other larger classes, it has been found quite possible to carry on the teaching of children in this manner, and the experience has shown that the scheme is not only a success, in that the condition of the eyes of the children under observation has remained as satisfactory as could be anticipated, but that it is a success from the attraction it presents to both teachers and

pupils. Both enjoy it, notwithstanding that for one of these parties—the teachers—the method calls for a degree of alertness and constancy of effort that is not the rule in ordinary teaching. An essential difference in the basis of the teaching required under this scheme was early demonstrated. The teachers found themselves cut off from the regular stand-by of modern teaching, whether of normal children or the blind—the book. They could no longer hand over a text-book to the children; they had to give out something from themselves and make their own conception of the lesson so definite that they could convey it to the child without adventitious aid other than the most primitive materials, chalk and a wall. They had to do real teaching. It was, therefore, no cause for wonder that in the beginnings the teachers themselves had to be shown how to do things, and the readiness, intelligence, and suggestiveness of their efforts in face of the difficulties of the makeshift conditions of the initial experiment have made it a success.

#### THE CLASS-ROOM.

The one necessity of a class-room for myopes is perfect natural illumination. The windows must be in such size in relation to the floor space that there is on an ordinary day at least 15 ft. candle illumination on the wall opposite the window and at a height of 4 ft. from the floor. The windows should be on the left-hand side of the children's desks; windows on the right-hand side in addition to those on the left are permissible if the sills are at least 6 ft. above the floor level; indeed such windows, or top lights, are an advantage in those rooms on account of the amount of handicraft work done in them. Windows on several sides of the room are objectionable unless they are placed high up in the walls, for they limit the available wall space for blackboards. The children must not sit facing the windows.

Artificial lighting for these rooms is a negligible consideration. All work other than drill, oral lessons, or games, is suspended immediately artificial light is required.

No special equipment other than table and blackboard provision is required. The ordinary school desk is unsuitable and a special desk<sup>1</sup> designed by myself has been in use since 1908 (figs. 1 and 2). The first batch was made by the pupils at one of the deaf schools. The desk has proved satisfactory and is now the ordinary equipment of these classes. It provides for each child a full-sized blackboard suitably sloped and

<sup>1</sup> The myope desk is made by Messrs. Hammer, of Charing Cross, London, W.C.

at a convenient height for sitting, and also a full-sized horizontal table for handiwork. It is convertible from one use to the other by merely lifting the board. Each room has fitted all round the walls a band of blackboard. The boards are fixed from 3 to 6 ft. above the floor



FIG. 1.

Desk in use in the myope classes, designed by the author, showing use as table for handicraft.



FIG. 2.

Myope desk in use as blackboard for free-arm writing.

level, so that they are available for both teachers and pupils without adjustment, and none is provided. In one school where the wall space is limited the writing surface is increased by the provision of continuous sheets of dull "oiled-baize" or "American cloth," this is fixed on to parallel rollers fitted to the wall; the black cloth runs over these rollers like a huge jack towel and gives a very large surface.

The use of a hall or a room clear of furniture is essential for the satisfactory working of these classes. Prolonged sitting or close work of any kind, even when it is so simple that it entails little use of the eyes, is bad for these children. For this reason none of the furniture of the ordinary class-rooms occupied by them is fixed to the floor; the myope desks and the chairs are easily moved to the walls and the floor space cleared. Further, a bare floor space permits of a variety of methods of teaching both useful and attractive, which cannot be undertaken in an ordinary class-room.

#### THE SIZE OF THE SEPARATE CLASSES OR FORMS.

The myope class comprises many separate classes, grouping children of the several standards of attainment and age. Each of these separate classes has a teacher, not necessarily one for each class, for the arrangement of the time-table allows of an alternation of the work of the teacher. When one group of children is taking oral lessons with the normal-sighted in the ordinary school, the teacher will be employed in giving lessons requiring writing, arithmetic, or manual work to another group. The number of children that any one teacher can deal with at the same time must of necessity be less than the same teacher could cope with in an ordinary school. Individual teaching is much more necessary for these children than for ordinary children, if only it be because there is the constant necessity of guarding against bad habits of stooping and peering at work. Further, the desk fitting—the combination blackboard and table—takes up the room of an ordinary twin desk. Experience shows that the greatest number any teacher can deal with successfully in any class working at the same subject and at the same time is twenty. But these conditions do not obtain at the present. The numbers of children are too small to afford such large groups of the same age and attainment, and in practice the teacher often has to run two separate classes, say of Standards III and IV, at the same time. Under these conditions twenty is too large a number. Twelve would be the optimum number. With that number of children the teacher

should be able to give to each child a fair share of individual attention, discover the particular difficulties of the child, and secure a result that could not possibly be approached under more crowded conditions.

#### THE CURRICULUM.

The photographs reproduced were taken at the experimental class three years ago, but they still give a very fair idea of the range of work undertaken.



FIG. 3.

This and subsequent photographs were taken at the first class, which has been working for four years. A lesson in physical geography in progress in a class-room of the ordinary elementary school. The front row is occupied by the myopes.

The oral teaching is taken with the normal children in the ordinary school with which the myope class is associated (fig. 3). By this means the myopic children are kept up to the standard of knowledge of their normal colleagues, have the benefit of mixing with them in class, and the oversight of the regular teachers. There is no difficulty in the arrangement, it is merely a matter of planning a convenient time-table, and the recognition by the teachers in the ordinary school of the particular difficulties of the short-sighted children. It has the added advantage that it keeps before the ordinary teacher the elementary

principles of the care of the eyes, which they are perhaps likely to forget when all the defective children are withdrawn from their care.

The literary work of the children is done in the myope class upon the blackboards provided for each child, and upon the wall-boards. The photographs give a very fair idea of the proper method of blackboard writing to be cultivated in these classes (fig. 4). The small script of thin white lines usually seen on the boards of the ordinary class-rooms and in lecture theatres is quite out of place in these classes. Letters must be large and the chalk lines broad and strong, and to secure this the chalk supplied should be square-edged and of double the measure of the stock size. The small desk blackboards are marked with white lines 2 in. apart, and the wall-boards 4 in. apart.

In the higher standards the want of some permanent record of the work of the children was felt; the essentially temporary character of blackboard work did not seem altogether satisfactory; mistakes were so easily corrected that carelessness was engendered. In the higher standards exercise books are being tried of a distinctly novel pattern. They are made up of large black paper sheets,<sup>1</sup> and the writing is done with white crayon, which gives a record of fair durability, but it can be wiped off if desired. The exercise books are clipped on to the desk blackboards, and the writing is done free-arm fashion as though on the blackboard, so that none of the dangers of ordinary writing, such as stooping over the work, are involved. The eldest of the pupils are allowed to make a permanent record of their work by printing. Two sets of printing types are provided for the use of each class. They are rubber-faced block-letter types, one of 1 in. height, the other of 2 in. height.<sup>2</sup> These are mounted on wooden blocks fitted with lateral pegs and holes, so that they can be joined together to form words. The words are set up and printed upon large sheets of white paper, the record is permanent, and goes to form a class library of scrolls which are useful for subsequent teaching. This device has done away with the necessity of invoking the aid of the professional printer to provide some form of literary matter which could be hung up in the sight of all the children and read with comfort by even the children in the back row. The printing itself is an admirable training in care and exactness, and is greatly liked by the children, in fact, it becomes one of the prize tasks of the class.

<sup>1</sup> Black paper exercise-books are provided by the British and Foreign Blind Association, of Great Portland Street, London, W.

<sup>2</sup> The rubber printing blocks are supplied by Mr. E. M. Richford, Snow Hill, London, E.C.

Drill and games enter largely into the time-table, and attempts are made to associate some of the games with the instructional work—e.g., large sheets of scenic canvas<sup>1</sup> are now supplied to two schools that have sufficient floor space, on these the teachers paint outline maps of different countries, marking out the position of the principal cities, rivers, mountains, &c.; the children walk about on the floor maps pointing with sticks to the different spots and marks, learning their geography by travelling it in miniature. With a teacher of resource such methods of instruction possess endless possibilities of interest.

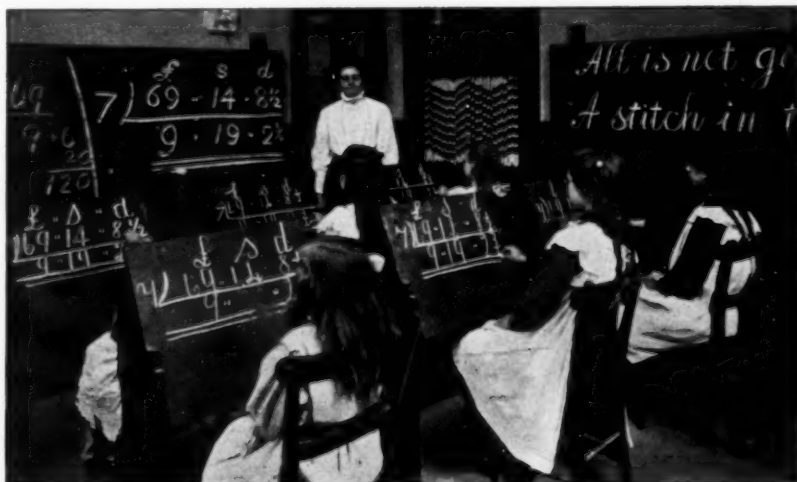


FIG. 4.

Arithmetic lesson in the myope class. The teacher uses the long wall blackboard, whilst each child has its own blackboard provided by the myope desk. Note the heavy strong lines of the chalk writing, and the bold upright characters. The ordinary thin-lined, straggly writing of the lecture theatre is quite inadmissible in these classes. Blackboard writing is an art to be cultivated.

The most difficult section of the work to arrange is the manual training. Whatever the work done it must be such that the fixed attention of the eyes is not demanded. For that reason all sewing

<sup>1</sup> The scenic canvas is obtainable up to 72 in. wide in two qualities; the better is known as long flax canvas, the inferior as jute canvas; one side is coated with ordinary white paint. It can be had from Messrs. William Good and Son, King William Street, E.C.



work is prohibited; it has been tried with a few of the elder girls but was quickly stopped. Knitting, on the other hand, fulfils the necessary conditions; a child that has any aptitude for it soon learns to do it automatically and with little use of the eyes; such children are allowed to practise it (fig. 5). The junior children (both boys and girls) are taught paper folding, stick laying, felt weaving in colours, and knitting. The seniors and some juniors are taught modelling maps, rough wood work where measuring can be done with rulers marked with minimum  $\frac{1}{4}$  in. marks. Advanced basket work is taught according to the advanced



FIG. 5.

Girls knitting. They are taught to work by feel and not by sight; only those who show an aptitude for the work are allowed to practise it.

scheme on workshop principles (but not including raffia work, which is too fine) (fig. 6). Bent iron work is satisfactory, particularly for boys; possibly also the netting of hammocks, tennis nets, &c. For the girls cookery and laundry of a simple kind, just sufficient to give an intelligent insight into the arts of housewifery.

The teaching of manual work to these children is not done with the same object in view that pertains to the teaching of the blind. With the latter the teaching is done with the view of the blind child subse-

quently earning a living by means of that particular work: basket-making, mat-making, and so forth. With the myopes it is quite different; these crafts are taught merely as a training in attention and care; it is not intended that any of them should enter into competition with the blind in doing these works; for that reason any particular work of this kind is not continued to the point where rapidity and skill is reached.

The scheme of education in view for the myopes is not merely technical but general. Many of these children are of high intelligence,



FIG. 6.

Children learning handicrafts. Any kind of work that will teach manual dexterity with the minimum of use of the eyes is admissible; no work that requires constant observation or the inspection of small parts should be taught.

and a good general training with special attention to the development of thought, initiative, a good bearing, and clear speech free from objectionable accent and idiom, will fit them for positions of usefulness and responsibility of the in-door and out-door type, such as small traders, collectors, agents, visitors, &c. This kind of occupation presents no risk to the eyesight.

The myopes drill in company with the normal children; they are also allowed to play with them so far as possible. But many of these

highly myopic eyes are very frail and unnaturally susceptible to injury. To give the teachers guidance in this matter lists are kept of the average and special cases. Those on the special list are limited in their games and drill to the mildest and least risky performances, and during school hours they do not play with the normal-eyed children.

#### THE ROLL OF THE SHORT-SIGHTED.

So far "myopes" have been written of as though they formed the total roll of these classes; they do not; one in every three on the roll is short-sighted because of the injury of some earlier keratitis or inflammation of the eye. The presence of these damaged children complicate the arrangements from an educational point of view, for they are rarely of the mental standard of the true myopes. But the classes are a great benefit to them. Cases of relapsing keratitis can rarely, if ever, be admitted to the ordinary school, for the mildest attempt at close work will usually induce a relapse. They do very well with the curriculum of these classes and get as much education as they are fit to receive or will ever be able to make use of. Further, they are under individual attention; the teacher learns what are the signs of an impending relapse, and the child is sent home on the slightest suggestion of a relapse; also under present arrangements the medical officer in charge has authority to order certain foods to underfed children (and cod-liver oil is included as a food), so that they are under better conditions than if they were left out of school altogether. There are also a small proportion of children with poor vision arising out of congenital effects. Any educational difficulties arising out of the inclusion of these children with the proper myopes will disappear as the provision for myope classes increases, and with it the possibility of better classification.

The list up to the end of 1912 is as follows :—

| Cause of defective vision                     | Boys | Girls | Total |
|---|------|-------|-------|
| Myopia ...                                    | 93   | 103   | 196   |
| Superficial keratitis ...                     | 16   | 34    | 50    |
| Interstitial keratitis ...                    | 7    | 17    | 24    |
| Disseminated choroiditis ...                  | 2    | 6     | 8     |
| Cerebral defect ...                           | 3    | 1     | 4     |
| Albinism ...                                  | 2    | 1     | 3     |
| Purulent conjunctivitis after exanthemata ... | 1    | 3     | 4     |
| Ophthalmia neonatorum ...                     | 3    | 6     | 9     |
| Cataract ...                                  | 4    | 2     | 6     |
| Coloboma uveæ ...                             | 2    | 1     | 3     |
| Aniridia ...                                  | 1    | —     | 1     |
| Buphthalmia ...                               | 1    | —     | 1     |
| Dislocated lenses ...                         | 1    | —     | 1     |
| Extreme hypermetropia ...                     | 2    | —     | 2     |
| Muscle defect ...                             | —    | 1     | 1     |
| Totals ...                                    | 138  | 175   | 313   |

## THE NECESSARY STANDARD OF VISUAL ACUITY.

For the successful working of such classes as these it is obviously necessary that children for whom this mode of education is proposed must have a reasonable visual acuity. In practice it has been found that it is desirable that the standard should be  $\frac{6}{18}$ . When the vision is less than this it is very difficult to prevent the children from peering and groping at their work, and the bad habits of a few will be copied by the many. Children when first admitted almost invariably have the bad habit of getting very close to their work, and the first lesson that has to be learned, and one that has to be the subject of constant reminders, is the necessity of doing all their writing and manual work at full arm's length. It follows from such a standard of visual acuity that all myopes must have satisfactory correcting glasses. Children for whom it is deemed undesirable to prescribe glasses have no place in these classes, but are fit subjects for the schools for the blind and partially blind. At the present time a number of children who have only  $\frac{6}{24}$  vision with their glasses are being tried, and it is possible that a fair proportion will be found suitable pupils when their mental intelligence is well up to the average.

## THE GRADE OF MYOPIA SUITABLE FOR SPECIAL TREATMENT.

Questions are frequently asked as to the grade of myopia which should indicate the necessity for special educational treatment. I am inclined to deprecate the setting up of any hard-and-fast lines of numerical limitation. Each case should be considered on its merits. So much depends upon the age of the child, the progress of the myopia, the fundus condition, and the existing educational attainment of the child. It is obvious that a child aged 7 with 5D. or 6D. of myopia is not to be compared with a child aged 13 with 8 or 9D. of myopia. The one is at the outset of its school career, the other at the end. The one case is suitable for immediate and radical change of its school work, the other may be sufficiently met by a modification of its existing school arrangements. So far as any indication can be given by diopters of myopia, it would seem that children with from 5D. to 15D. of myopia are suitable subjects for these classes. Those with less than 5D. are fit for the ordinary school with special precautions, such as those indicated under the heading of "Easy treatment as regards eye work"; those with more than 15D. are suitable for education in the schools for the blind

and partially blind (with the possible exemption from Braille teaching), unless the fundus conditions are fair and the vision, with a suitable correction, is so good that they can safely take advantage of the myope class. In any case there can be no doubt that as the knowledge of the existence of this scheme of education becomes widespread and sufficient provision for reported cases is obtained, there will be a much greater demand for special educational treatment than at present. And it is possible that the range will be extended downwards, especially for cases of myopia occurring in the earlier years.

#### REGULAR MEDICAL SUPERVISION.

The children who are in these classes are regularly examined by an ophthalmic surgeon at intervals of six months. Each child is examined in a dark room, the refraction worked out and the fundus condition noted. Subsequently the vision with the glasses being worn, or with any alteration suggested by the previous objective examination, is recorded. The records are kept in a card index and are ready for reference in any inquiry concerning the work and progress of a child. The result of these repeated examinations was the subject of a paper recently read before the Ophthalmological Society of the United Kingdom,<sup>1</sup> and in that paper will be found details of the mode of recording the fundus conditions and the degree of change in the myopia of eighty children over a period of years. The importance of the systematic examination of the eyes of these children cannot be overestimated.

The medical officer in charge also exercises a supervision over the educational work of the children. He suggests or inquires into the advantages and possible risks of new methods of work. And in particular he indicates to the teachers those children whose eye conditions are such that they may not do any work entailing the least degree of strain, or join in games or drill in which there is any risk of blows to the face or head. For such the freedom of the playground, common to the whole elementary school, is prohibited; they must play in their own limited area.

In conclusion, the lessons of the experimental establishment of these classes and their extended working are: That a suitable system of teaching myopes can be arranged and carried out successfully. That such classes should never be independent units, nor be associated with

<sup>1</sup> Harman, "An Analysis of 300 Cases of High Myopia, with a Scheme for the Accurate Record of Fundus Conditions," *Trans. Ophthalm. Soc. U.K.*, 1913, xxxiii, pp. 202-220.

existing blind schools, but be formed as integral parts of existing elementary schools. That their success depends almost wholly on the intelligence and initiative of the teacher, who has to do real teaching and not merely to act as a pedagogue to lead the child to the school book. That the training for these children should be general and not merely technical. That classes for these children should be of small size with an optimum number for each teacher of a dozen, but never more than a score. That there must be a standard of visual acuity of  $\frac{6}{18}$  vision for the children to successfully take a share in the work. That the children must be under regular individual supervision during the whole of their school life.

### **Glaucoma associated with Venous Congestion.**

By A. FREELAND FERGUS, M.D.

THE subject of glaucoma is, at present, receiving much attention alike from pathologists, physiologists and operating surgeons. I desire in this short communication to bring to the notice of the Society cases which I think must be attributed to some changes in the vascular system, probably of the nature of sclerosis in the small veins. Far be it from me to pose as an authority on the pathology of glaucoma. Till the case which I am about to show you to-night came prominently under my notice I, for the most part, held, as I still do, to the theory of obstruction of the filtration angle. Now, unquestionably, high tension and obstruction at the filtration angle are such frequent concomitants that it is almost impossible not to regard them as cause and effect. Still, the cases which I wish to bring before you to-night, of which the most important is that of J. G., show quite distinctly that high tension can exist without any adhesion of the root of the iris to the posterior surface of the cornea, but, on the contrary, with an enormous increase in size of the filtration angle.

J. G. first came to the Glasgow Eye Infirmary on January 13, 1911, and was diagnosed as a case of separation of the retina. At that time there was no suspicion whatever of tumour. The separation was extensive but the tension was normal and the eye transilluminated. He was not seen again by me till January 13 of this year, when he returned, and now it was found that in addition to the separation the

tension was +2. Under these circumstances I thought it but prudent to enucleate, and accordingly did so on January 16. After operation the eye was sent to Dr. Logan Taylor, Pathologist to the Eye Infirmary. He at once found that there was no tumour, but a very extensive separation of the retina with cupping of the optic nerve to a depth of nearly 2 mm. The important point in this case is the unusual size of the canal of Schlemm and the enormous distension of the corneo-iritic angle. Now, it seems to me from the dilatation of the canal of Schlemm and also of some of the other veins that we have here evidence of an obstruction in the venous circulation. That may or may not have given rise also to the separation of the retina. The high tension in this case is certainly not due to any obstruction of the corneo-iritic



FIG. 1.

Case of J. G. Section showing extensive separation of the retina.

angle but is unquestionably accompanied by its enormous dilatation. I have never been satisfied that the characteristic dilatation of the deep veins of the conjunctiva is due to high pressure in the eyeball, and I think this case abundantly shows that that dilatation may indicate venous obstruction and may be the cause rather than an effect of the malady.

A somewhat analogous case is that of Mr. A., whom I saw in January of the present year. His left eye was completely blind from glaucoma, the tension being +2 and the nerve deeply cupped. The sight had gradually diminished during the past six years and the eye had been completely blind for the last year. The vision of the right eye was up to Snellen's full standard. The appearances in the right eye are



as in health and the field of vision is normal. The important point in this case to me was that the veins in the eye that was affected were at least twice their normal size. Each vein was nearly three times the size of the corresponding artery. Here we have, unquestionably, evidence again of obstruction in the veins. In the case of Mr. A. there was very considerable congestion of the deep veins of the conjunctiva.

Lastly, I have twice in my lifetime enucleated eyes that had become painful on account of glaucoma, the patients subsequently succumbing from cerebral neoplasm. One of the cases was that of an elderly lady who had suffered from attacks of high tension for a considerable number of years. When I first saw her she had far advanced chronic glaucoma.



FIG. 2.

Case of J. G. Showing dilatation of the canal of Schlemm and of the filtration angle.

The eyeball was intensely painful and was perfectly sightless and had been so for some years. Under the circumstances I thought enucleation desirable and accordingly performed the operation. After the lapse of a few weeks she went home. I happened to be some months afterwards in the town in which she lived and called to see her. Her remaining eye kept healthy, but she suffered much from vomiting and severe headache, and for that condition was being seen regularly by her ordinary medical attendant. A few months afterwards I saw a notice of her death, and on inquiry discovered that she had died of a cerebral neoplasm. Unfortunately no autopsy was obtained.

166 Fergus: *Glaucoma associated with Venous Congestion*

Since writing the above, I have seen in the *Archives of Ophthalmology*<sup>1</sup> an interesting account by Dr. Stähli, of Zurich, of the pathology of hæmorrhagic glaucoma. G.'s case was certainly not an ordinary case of hæmorrhagic glaucoma. As far as I saw there never was a hæmorrhage on his retina, but a large separation. The fluid between the separation and the choroid was not ordinary blood, so his case cannot be called hæmorrhagic glaucoma in any ordinary sense of the term. In two of the three cases which Stähli records there is marked sclerosis of the central vein, but no thrombosis. I think Gardner's case is probably of the same nature. Stähli's paper contains a valuable bibliography of the subject.

<sup>1</sup> *Arch. of Ophthalm.*, New York, 1913, xlii, pp. 248-55.

PROCEEDINGS  
OF THE  
ROYAL SOCIETY OF MEDICINE

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VOLUME THE SIXTH

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COMPRISING THE REPORT OF THE PROCEEDINGS FOR THE  
SESSION 1912-13

OTOLOGICAL SECTION



LONDON  
LONGMANS, GREEN & CO., PATERNOSTER ROW  
1913

## Otological Section.

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*Corrigenda.*—On page 59, line 10, for "of these twenty-seven were . . ." read "of these twenty, seven were . . ."; on page 60, line 1, for "Lenvai Prize" read "Adam Politzer Prize."

The Council think it right to state that the Society does not hold itself in any way responsible for the statements made or the views put forward in the various papers.

## Otological Section.

October 18, 1912.

Dr. J. DUNDAS GRANT, President of the Section, in the Chair.

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### Lateral Sinus Thrombosis; Serous Meningitis; Recovery.

By DAN MCKENZIE, M.D.

MALE, aged 25, with middle-ear suppuration (left) of fourteen years' duration, came to hospital on January 10, 1912, with pain in and around the ear, vertigo and rigors; temperature oscillating between 100° and 104° F. Some stiffness of the neck on the left side, slight nystagmus, especially towards the left. Polypus in the left meatus. Scars of old operations over the mastoid process.

January 11: Mastoid operation; fissure in posterior meatal wall led into a very large cavity full of cholesteatoma. When cleared out the following structures lay exposed: Behind,  $\frac{1}{2}$  in. of the lateral sinus, covered with granulations, and a circular area of the dura of the posterior fossa medial to the lateral sinus; in the tympanic region, the facial nerve was exposed from the genu to near its exit at the stylo-mastoid foramen. The nerve was covered with granulations, and the meatal polyp previously noted was found to be attached to it. The posterior meatal wall was destroyed as far out as the cortex. I fully exposed the dura of the posterior fossa by removing the papyraceous bone that covered it; it bulged somewhat. The lateral sinus was opened and cleared of clot upwards until blood flowed freely. Pus was seen welling up from the bulb.

January 15: Pyrexia and rigors continuing, the jugular vein was tied and resected in the neck, and the lateral sinus groove opened inwards towards the bulb.

January 16: Severe occipital headache and slight head retraction. Nausea. Pulse 60, very irregular. Respirations 14. Temperature 98° to 102.6° F. Dynamometer: Right 142; left 112. Slight spontaneous nystagmus to both sides. The exposed dura of the posterior fossa, which was now markedly bulging and pulseless, was opened by a long incision without any anæsthetic. Cerebrospinal fluid under tension. Cerebellum explored with scalpel without result.

January 19: Meningeal symptoms but little relieved. Under chloroform, labyrinth opened and wire drain inserted in internal auditory meatus. In the outer labyrinth wall, deep to the facial nerve, the cholesteatoma had made a considerable excavation, with the nerve strung across it. This excavation had been shut off by bone formation from the rest of the labyrinth.

January 20: Facial paralysis observed after operation.

January 20-24: Temperature oscillating between 97° and 102° F. Pulse and respirations averaged 80 and 16 respectively, and the meningeal symptoms moderated. Hernia of the brain at the dural opening. Wire drain, which did not act well, removed.

January 25-27: Temperature normal. Meningeal symptoms absent.

January 29: Temperature rose to 101° and 103° F. Meningeal symptoms recurred. Lumbar puncture; 1 oz. of cerebrospinal fluid withdrawn. Examination: "Leucocytes numerous; a few lymphocytes. No bacteria. Albumoses. Nucleo-globulins well marked. Wyatt Wingrave."

January 31: Temperature normal again.

February 2: Temperature rose to 102° F., with a reappearance of headache, and occasional irregularity in the pulse. Lumbar puncture; 2 dr. removed.

February 5 and onwards: Temperature normal. Progress uninterrupted.

The hernia has disappeared; the facial paralysis remains; the post-aural wound is still open, awaiting a plastic operation.

The prompt fall of temperature and disappearance of meningeal symptoms on two occasions after lumbar puncture is not the least interesting feature in the case. I have recently had a similar experience in another case with occipital headache and malaise, without fever, following a labyrinthotomy for suppuration.

## DISCUSSION.

Mr. HUNTER TOD desired to ask why the jugular vein was not tied and resected at the first operation. There seemed to have been every indication for doing so; the symptoms were typical, and pus was said to have been welling up from the bulb. The subsequent condition of the patient was, he thought, partially due to the operation not having been completed at the first occasion. From his own personal experience of over seventy cases, he was sure the best results were obtained if the big operation was done straight away, rather than postponing part of the operation, although in this particular case the recovery of the patient reflected credit on the operator. He would also like to know why it was necessary to go through the labyrinth to drain the internal meatus. If he had operated on the case he would have resected the jugular in the first instance, and if meningeal symptoms arose, he would have incised the dura mater. By removing the bone in front of the lateral sinus, towards the semicircular canals, and then exposing the brain surface freely, the infected area could be well drained. If symptoms pointing to internal ear trouble afterwards arose, then he would open up the cochlea. In septic cases it was risky to drain through the internal ear.

Dr. MILLIGAN said he had intended to ask the same question that Mr. Tod had done. The welling up of pus from the bulb was an indication that the deep part of the vein, and probably the bulb also, was involved, and he thought it would have been advisable at that moment to have ligatured the internal jugular vein. He also asked what was the reaction of the cerebrospinal fluid. Clinically, it was very important to know whether it was alkaline or acid. The normal reaction was alkaline, but if meningitis was passing from the serous to the purulent variety, the alkalinity diminished, and the reaction became acid.

Mr. ALEXANDER SHARP said Dr. McKenzie was to be congratulated upon having so ably piloted this difficult case into safety. He asked whether the cerebrospinal fluid was removed as a therapeutic measure, or for investigation. If the former, the amount seemed to be too small to be of value. Sinus cases often produced surprises. Sometimes the classical symptoms were present, yet the surgeon found no sinus disease; at other times there might be no reason to suspect sinus disease, but it was there. He was asked to see a patient suffering from an ordinary furunculosis. On seeing her again a month later there was a diffuse inflammation of the external meatus with stenosis of the canal. The only symptom had been intense earache, which occurred every night and lasted for about three hours. Temperature and pulse normal. No previous fear trouble. On operating, pus was found in the middle ear, the mastoid antrum and cells were congested, and on exposing the lateral sinus about  $\frac{1}{2}$  oz. of a milky fluid welled up. Convalescence was uneventful. There seems to be need for revision of the signs and symptoms associated with sinus disease. In this case there was nothing to suggest that condition.

Dr. McKENZIE replied that he sympathized with what Mr. Tod and Dr. Milligan had said in regard to the labyrinth, but the case was an extraordinary one, the cholesteatomatous cavity being the largest he had ever seen. Amongst other organs invaded by the cholesteatoma was the labyrinth; there was a comparatively deep recess behind the facial nerve, and he concluded from the appearances that the labyrinth was destroyed, and that his surgical measures would make no difference to the state of matters there. But it turned out to be one of the cases described, in which the slowly advancing disease was met in the labyrinth by the formation of an osseous barrier. When he broke into the labyrinth through this wall, he came upon clear labyrinth fluid: there was no suppuration of the labyrinth. He had not considered making labyrinth tests, because at the first operation he believed that the labyrinth was seriously involved. The question of tying the jugular had been raised many times in connexion with these cases, and some people had a tendency to delay ligature until it was seen whether the opening of the lateral sinus had not removed the danger. He had waited a couple of days in this case, and as the symptoms showed that the danger was not removed, he tied the jugular. He did not think the delay made any difference to the meningeal symptoms. The cerebrospinal fluid removed on the second occasion was as much as could be got to flow.

### Case of Epithelioma of the Meatus.

By DAN MCKENZIE, M.D.

MALE, aged 52. Suppuration of middle ear (left) for twenty years. Pain and facial paralysis came on a month before his first attendance at hospital. The fleshy and tender nature of a polypoid growth in the meatus raised a suspicion of malignancy, which was confirmed by the microscope (epithelioma). An attempt was made to remove the growth. A post-aural incision was made, and the typical mastoid operation performed; thereafter the membranous meatus and all the walls of the bony meatus were freely removed. The middle ear showed granulation of the usual purulent type; the apparently malignant growths seemed to be seated in the meatus, which was cut across close up to the auricle. Recurrence was observed six weeks after the operation, and the disease has made considerable advance since. The trend of the disease seems to be towards the outside, herein differing from epithelioma of the tympanum, in which the disease tends towards the nasopharynx.

**Carcinoma of the External Ear.**

By W. MILLIGAN, M.D.

E. L., MALE, aged 65. Ten months previous to admission to hospital complained of a dull, smarting pain in the upper part of his external ear. A small hard nodule formed upon the free border of the helix. This broke down and ulcerated. On admission the external ear presented the appearances as seen in photograph (photograph shown). Several of the peri-auricular glands were enlarged, but apparently were not malignant. Operation advised. Auricle removed. (Macro- and microscopic specimens shown.)

**Malignant Disease of the Middle Ear—Invasion of Mastoid Area and Parotid Gland.**

By W. MILLIGAN, M.D.

A. T., MALE, aged 20, had suffered from post-scarlatinal suppurative otitis media since the age of 3. On admission to hospital the external meatus was found blocked with a greyish, sloughy-looking polypus. Complete left-sided facial paralysis. Hearing power upon affected side *nil*. History of repeated attacks of vertigo. Slight oedema over mastoid process and displacement of auricle. Swelling in front of tragus. Mastoid cells opened and found to be invaded by growth, apparently springing from inner wall of middle ear. Fallopian aqueduct eroded and facial nerve found degenerated. Horizontal semicircular canal eroded. Growth removed as completely as possible. Post-auricular wound left open. Is light treatment advisable or are injections of Coley's fluid worth trying?

**DISCUSSION.**

Dr. MILLIGAN said he would be glad to have the specimen submitted to the Morbid Growths Committee of the Section. The report which he received from the clinical laboratory of the Infirmary was that it was carcinoma. He wished to know from whence it originated. There was a history of prolonged suppuration from the middle ear; possibly it was a growth of the parotid gland which had invaded the middle ear. There was not much pain complained of.

The PRESIDENT (Dr. Dundas Grant) said his experience was that when such a growth began in the temporal bone there was always considerable pain. This would seem to support the idea of origination in the parotid gland in the present case.

Dr. DAN MACKENZIE remarked that Dr. Milligan said that the clinical history suggested that it grew from the middle ear, and yet subsequent recurrence of the growth was outwards.<sup>1</sup> Mr. West and Mr. Scott had pointed out that the ordinary growth of malignant disease in the tympanic cavity was inwards towards the nasopharynx. This suggested that the growth had originated external to the tympanic cavity. He was showing that day a case in which the disease seemed to have sprung from the membranous meatus. It was removed, and the recurrence had tended outwards, as would be expected in mental cancer.

### **Bilateral Attic Disease.**

By F. F. MUECKE, F.R.C.S.

PATIENT is a male, aged 40. Acute otitis in both ears ten years ago. There is necrosis and perforation of the outer bony walls of both attics; left drum also shows a depressed scar. Bone-conduction normal in both ears. Whisper, 2 in. to 3 in. in both ears. Slight suppuration still present.

### **Epithelioma of Auricle and External Auditory Canal.**

By HUNTER F. TOD, F.R.C.S.

FEMALE, aged 76. The fragus was removed by operation over four years ago; treatment also by X-rays and radium. A polypoid growth now fills external meatus, and a superficial ulceration is spreading outwards along the concha.

Does the age of the patient and the slowness of the growth contra-indicate an extensive operation?

<sup>1</sup> Note.—Dr. Milligan did not say that the growth had recurred. Only one operation had been performed, and that for removal of the primary growth.



DISCUSSION.

The PRESIDENT pointed out that there seemed to be no vacuolation in any of the cells, such as one had been taught to recognize in rodent ulcer.

Dr. URBAN PRITCHARD, discussing the question of operation, said that in view of the fact that the patient was old and feeble he did not think operation was advisable.

Mr. A. CHEATLE thought the patient should have the benefit of operation : she was in good health and might live another ten years if it were done.

The PRESIDENT agreed that something should be done for the patient in the way of operation. There was no glandular involvement, and the tumour was of quite slow growth.

Mr. TOD replied that the patient was nearly cured by radium last February, but she left the hospital too soon. He had not seen her until recently. He wanted advice as to whether he should curette out the ear and apply radium, or whether a more radical operation should be performed. In favour of the simpler method were the age of the patient, the long duration and slow progress of the disease, and the fact that a cure had already nearly been obtained by this method. In favour of the more radical operation were the complete elimination of the disease and the avoidance of intense pain at a later stage of the disease, which would occur if no operation were performed.

**Epidiascopic Demonstration of X-ray Negatives of Normal and Pathological Temporal Bones.**

By W. MILLIGAN, M.D.

DR. MILLIGAN had been engaged along with Dr. Barclay with X-ray photography of various pathological conditions, especially ear disease, and was bringing observations before the Section so as to receive hints as to how the method could be perfected. The slides, although good *negatives*, were somewhat difficult to interpret on the screen. At the Manchester Royal Infirmary they had been making skiagrams of every case of chronic suppurative otitis media submitted for operation independently of the diagnosis which had already been made. Speaking generally, it had not thrown much light on the clinical diagnosis, but there had been occasions when the skiagram had saved an operation. A patient attended with acute middle-ear suppuration, and considerable pain about the ear, perhaps with œdema and periostitis. The instinct was to conclude that there was pus in the mastoid cells, and straight away to operate. But in some such cases the mastoid cells had been

## 8 Milligan: *Epidiascopic Demonstration of X-ray Negatives*

unaffected, and the case was one of pure periostitis. The radiographing of mastoids was certainly very difficult; the radiographer must be expert, and the patient very quiet, as the slightest movement vitiated the picture. There was at present a lack of unanimity as to how the patient should be placed, and what focus tube should be used. At the Infirmary they had placed the patient prone on the table, and turned the head round to an angle of  $90^{\circ}$ , the head being put on a platform of wood, which was inclined at an angle of  $25^{\circ}$  with the horizontal. The plate was placed under the affected ear, with the focus tube about 9 in. above the head, and so placed that the centre of the focus tube struck a point an inch above the highest point of the pinna. Dr. Logan Turner was in favour of the patient's auricle being drawn away from the mastoid when the skiagram was taken. That had been tried, but had been given up. If the mastoid was inflamed and tender, it was difficult to get the patient to allow the auricle to be drawn forward and kept there when he was lying on a hard substance. Even if the auricle came into the picture it was easy to disregard it with the eye, and read what was deeper. The X-ray photograph should be taken from *both* sides so as to have the contrast. If one had a sufficient number of X-ray plates, and studied them carefully, he thought it was possible, from plates alone and without seeing the patient, to know whether that person had a normal mastoid or had acute or chronic mastoiditis. There were sufficient points, notwithstanding the variation of the negatives, to enable one to differentiate. It was also useful in determining the amount and extent of malignant disease in and around the ear. He showed a picture of malignant disease of the ear where the growth could be seen invading the deeper part of the bone, where one had not been inclined to operate, but had operated in order to relieve tension and pain. The negative should always be examined dry, as it then showed the detail much better than when wet. The principal points were that in an acute mastoiditis the general mastoid area was obscured; in chronic mastoiditis it was often quite opaque. The position of the lateral sinus groove was very important. In a normal temporal bone the X-ray photograph scarcely showed the lateral sinus at all; but in acute mastoiditis one could see the outline of the groove, while in a chronic case it came out very distinctly. He could not say anything very definite about the petrous bone. In one or two instances they thought they had sufficient evidence to diagnose tubercular lesions in the petrous; there had been lesions there, but he was not sure that it was

a correct interpretation beforehand. He had had the case of a child with both ears externally deformed; no meatuses at all, and the parents were anxious to know whether anything could be done. It was only 6 weeks old. His reply was that the child should be taken to the radiographer, to see if there was a labyrinth. The result was that though there was a labyrinth it was so badly developed that it was considered that no operative treatment would be of any practical value.

### Left Otorrhœa and Right Temporal Sphenoidal Abscess.

By RICHARD LAKE, F.R.C.S.

THE patient, a male, aged 39, was a gardener by occupation. Previous history: Never had any serious illness, but he has had an offensive discharge from the left ear for many years.

May 14, 1912: First seen by Dr. Charles Wade, of Boscastle, Cornwall. He complained that on May 10 and 11 he had been very weary, and on May 13, when rising in the morning, complained of giddiness, and was sick after taking a dose of Epsom salts. He was repeatedly sick for some days and suffered much from giddiness. The bowels were obstinately confined. Temperature 97.4° F.; pulse 60.

So he continued more or less until May 22, when Mr Lake found him with a temperature of 103° F., and pulse 68. The discharge from the left ear was free and offensive, and remained so till May 26, when it gradually became less, and by June 4 it was scarcely perceptible. The ear had been regularly syringed with a solution of lysol. Since that time he had had little or no pain. The bowels had not been opened since May 30, but three stools were passed between May 27 and 30 which were quite characteristic of enteric. The urine was passed involuntarily.

On May 29, 30, and 31 there was much quiet muttering delirium, with subsultus tendinum and carphology.

The pupils had always been equal and reacted alike; disks normal, no paresis of any part. On May 30 some blood was taken and sent to the Clinical Research Association for a Widal reaction; the result was negative. There have been no suspicious spots. The spleen has not been felt, and pulse never exceeded 74, nor showed any irregularities. There have been no pulmonary symptoms. (The date of this report is June 4.)

10 Lake: *Otorrhea and Temporal Sphenoidal Abscess*

The patient was admitted to the Royal Ear Hospital on June 5. He was examined by Dr. Bernstein with a view to deciding whether there were any symptoms of cerebral or cerebellar abscess, but none was found. The eyes were also examined by Mr. Lyle, and the disks were found to be normal. On June 6 a radical mastoid operation was performed on the left side, and a patch of caries was discovered in the region of the superior horizontal canal. This was scraped out, and the labyrinth opened up and found to contain pus. No stapes were present. As there was no indication for further exploration, nothing further was done.

The patient seemed relieved by the operation, and was markedly better for two days, when the temperature began to rise again in the morning, falling towards night; never, however, getting above 101° F. His general symptoms seemed to point to the presence of pus somewhere in the cerebrum. On June 12 an exploratory operation of the brain was performed, and the middle fossa opened out and explored in every direction. No pus was found; the dura bulged and did not pulsate. On incising the dura a large amount of serous fluid escaped. This was cleared. A large amount of serous fluid escaped, however, when exploring towards the fissure of Rolando. It should be stated that an investigation of the cerebrospinal fluid on June 12 showed moderate lymphocytosis, no pus cells, and a very few epithelial cells.

The patient's condition became steadily worse, and further exploration was made on June 16, when a further large amount of fluid was removed from the same situation as previously. There was now distinct pulsation of the brain tissue. No anæsthetic was used for this operation, as the patient was only semiconscious. On June 17 he had a fit at 9.15 p.m., which started with a spasm in both eyes and left arm; no movements to the right. The right arm was slightly contracted, but the left was flaccid. The wound was opened up, the plugging removed, and the wound was cleansed. A considerable amount more fluid, tinged with blood, was released from the same situation as before, and a rubber drainage-tube was passed to enable it to flow freely. There was a slight spasm of the eyes and both arms, but especially the left arm, just as the patient was being removed from the table.

The patient died on June 18, the temperature having risen to 104° F.

There had never been any opportunity of making a thorough examination of the patient, as from the very time of his admission he was not sufficiently rational to be able to answer questions intelligently, and he was more often unconscious and suffering from delirium, combined with subsultus, than not.

## DISCUSSION.

Mr. LAKE added, that at the post-mortem was found a right temporo-sphenoidal abscess, also a non-suppurative infarct in one lung, the size of a five-shilling piece. Also, over the right temporo-sphenoidal area there was a patch of recent suppurative meningitis.

Mr. HUNTER TOD asked if there was any disease of the right middle ear. He could not believe that the temporo-sphenoidal abscess on the right side was due to the middle-ear suppuration on the left side. If it were possible for a temporo-sphenoidal abscess to occur on the opposite side of the ear, it was a matter of great importance, because hitherto one had been taught that if only one side was infected, intracranial affection on the other side could be excluded.

Dr. MILLIGAN asked whether it was not possible that the temporo-sphenoidal abscess had its infection from the lung? One knew that brain abscess was not altogether uncommon in cases of pulmonary disease. Possibly the infection in this case occurred at the time the patient had the infarct in the lung.

Mr. KISCH suggested that the case was really one of malignant endocarditis; that would explain the presence of the infarct, and abscess.

Mr. LAKE, in reply, said he had no explanation to offer, but he had brought the specimen. As the kidneys and other organs were normal he did not think it necessary to mention them; the post-mortem examination was a complete one. There was no suppuration in the infarct, and the relationship to the cerebral condition might be direct or indirect.

**A Simplified Apparatus for Inflating with Heated Air.**

By P. MACLEOD YEARSLEY, F.R.C.S.

MR. YEARSLEY remarked that a good deal had been said and written on the Continent during the last two or three years about the use of heated air, inflated through a catheter, but most of the apparatus for the purpose were somewhat clumsy, and many of them were heated by an electric lamp. The best and simplest, so far, had been one shown by Dr. Andrew Wylie at the British Medical Association Meeting at Birmingham last year. That apparatus he had recently modified with the idea of making it simpler and lighter for use. It consisted of an inflating bag having an aluminium chamber, with a lining of asbestos to prevent over-heating. Inside the chamber was a small cautery

## 12 Yearsley: *Simplified Apparatus for Inflating with Hot Air*

burner, and on the other side a nozzle for placing in the catheter. Below was a switch and plug with cords attached to the battery. It was a collar switch, which put the current on quite easily by pushing upwards. It was sufficiently light to use like an ordinary inflating bag. He had been using it for six months, and it heated the air very comfortably and sent it direct into the catheter. Krohne and Sesemann were the makers.

### DISCUSSION.

Mr. HUNTER TOD asked if Mr. Yearsley had tested the temperature of the air at the other end of the catheter when he used his instrument. He had found that even  $\frac{1}{2}$  in. from the end of the catheter the temperature of the air was not raised, and he did not therefore think one could get warm air into the middle ear by means of the catheter. He quite admitted that the warm air as it passed out of the catheter gave a sensation of comfort in the throat, but he thought that the good results considered to be obtained from hot air treatment were due to the simple inflation of the ears rather than to the hot air itself.

Dr. H. J. DAVIS said that when the dentist blew hot air on to one's tooth to dry a cavity before filling it was not always very comforting. Heating the end of the hot-air syringe heated the air passing through the cannula.

Dr. WATSON-WILLIAMS said that unless there was perforation of the drum he did not see how the hot air could get well into the ear up the Eustachian tube. Even if it came out hot at the end of the instrument the volume of air was increased in the middle ear by politzerization or catheterization, and that gave a sense of inflation.

Dr. KELSON said he had used the method for six or seven years, and he disagreed with Mr. Tod's remark. There was certainly hot air at the end of the catheter, and when patients said it was hot in the ear he had no reason to disbelieve them. A difficulty with apparatus was usually the weight, but he had been using a modified dentist's design with good results. The point to be careful about was not to burn the patient's nose, and that could be obviated by having a fibre catheter. Certainly in cold weather it was more grateful and beneficial to patients than blowing in cold air.

Mr. YEARSLEY replied that he would be pleased to give a demonstration some time. The air was hot even 2 in. in front of the catheter, and patients said the air was heated. As to results, beyond increased comfort to the patient, he was bound to say he had not yet observed them. He designed the apparatus to see whether there was any therapeutical effect from the hot air, but he had found none.

**Capillary Angioma of the Right Membrana Tympani.**

By E. A. PETERS, M.D.

M. H., AGED 48, labourer. Capillary angioma of the posterior upper quadrant of the right membrana tympani; the region of the malleus is involved. The lower part of the right face, including the lobe of the ear and the auditory meatus, is affected below a line drawn from the auditory meatus to the mouth. The right side of the palate and tongue are also marked. The patient has been deaf for about twenty years. No evidence of syphilis can be traced.

Stop watch: C on mastoid, -20 seconds right and left; C<sup>4</sup> on mastoid, -2 seconds right and left. Tuning fork: 32 vibrations per second on mastoid, -12 seconds right and left.

**A Horsebean removed from the Middle Ear during a Radical Mastoid Operation for prolonged Otorrhœa in a Boy, aged 9; with two Sequestra, containing the Outer Wall of the Canal of the Facial Nerve.**

By H. J. DAVIS, M.B.

THE boy was brought to the hospital with a history that "polypi had been removed from the ear on several occasions, but they quickly returned." It was evident that the mastoid was extensively involved



Horsebean and two sequestra removed from middle ear.



and he was operated on at once. The mastoid process, the interior of which was bathed in pus, came away entirely, and the facial nerve could be seen lying on the digastric muscle. The middle ear was occupied by a foreign body, which was surrounded by granulations and proved to be a horsebean which was germinating. The history points to the foreign body having been there about four months, but the boy never mentioned the fact. The wound healed rapidly, but facial paralysis was present and this should recover.

The specimens were mounted by Dr. Elworthy.

### A Case of Non-infective Meningitis Five Months after Cerebral Abscess.

By W. M. MOLLISON, M.C.

W. H., AGED 9, attended the aural out-patient department at Guy's Hospital on March 10, 1912, suffering from headache and left otorrhœa and a squint. His mother had noticed the squint for six weeks, and indeed the boy had been so ill (vomiting and headaches) that she had kept him in bed but had not sought medical advice. The otorrhœa was very profuse, pus filling the meatus three times after removal in the space of an hour. The squint was found to be due to weakness of the right external rectus. Mr. Eason examined the eyes and reported advanced optic neuritis in both eyes. There was a little swelling over the mastoid process and slight displacement of the auricle.

Operation was performed; cholesteatoma was found in the antrum and the tegmen antri was eroded, and a nipple-like projection of dura projected into the antrum; pus was seen coming from this. A crucial incision was made into the dura mater and the abscess opened; an ounce of thick, foul-smelling pus was evacuated, a double rubber tube put in, and the wound packed with gauze. A small hernia subsequently appeared but was cut off, and the boy made a good recovery, though the cavity was difficult to deal with on account of the bulging down of the dura mater.

In August last the boy complained of headaches and tenderness about the meatus, and on August 22 the headache was very severe and the boy was drowsy, and the temperature was 101.5° F. and pulse 120. He was again admitted. There was still a small sinus behind the auricle and the dura was bulging down so as to fill the meatus. Incision

over the old wound showed the dura mater bulging over a small cerebral hernia; it was incised but no pus found. A lumbar puncture was now performed, and the cerebrospinal fluid was discovered to be markedly opalescent; obviously meningitis was present. The dura mater was now freely incised (after removing a considerable area of bone) and strips of gauze inserted under it in several places. The immediate result of the operation was great improvement in the patient's condition; in a few hours the pulse fell to 84 and the headache disappeared; 10 c.c. of a polyvalent antistreptococcal serum were given under the skin. Lumbar puncture was repeated twenty-four hours and forty-eight hours after operation, and three or four pints of normal saline were given.

Bacteriological examination of the fluid was carried out three times and cultivations remained sterile after three days' incubation; the fluid contained large numbers of polymorphonuclear cells. Several examinations failed to reveal any organism. The fluid finally became quite clear, and the boy recovered completely.

#### DISCUSSION.

Dr. H. J. DAVIS said that just before the Boston meeting he was afflicted with a similar case, but somewhat worse than this. He took photographs of the case over to Boston and asked the opinions of several as to what should be done. The hernia was as large as an apple. Some said it should be cut off, others that it should be left alone. Mr. Ballance advised him to leave it alone and it would disappear. When he got back it was healed over. He would show the case at the next meeting.

Dr. MILLIGAN suggested that graduated pressure should be applied to the hernia by means of a lead plate. Repeated lumbar punctures might assist the result.

Dr. PETERS said it might be possible to use celluloid collodion, which could be supplemented by lumbar puncture. That failing, pressure could be made as Dr. Milligan advised.

Mr. HUNTER TOD remarked that cerebral herniæ did not always disappear if left alone. Seven years ago he showed a boy with a large cerebral hernia with granulations. Some advised that it be cut off, others said pressure should be applied. He did nothing. Later the boy got erysipelas, and after that the skin grew over it, but the hernia had remained. Otherwise, the boy was quite well. In the cases in which he had tried to remove the hernia he found the skin very closely adherent to the surface of the hernia. In one case the patient died soon afterwards from meningitis. In another case, in which he

was successful, he separated the skin from the edge of the hernia, and exposed its bony margin. More bone was removed, so as to make the opening into the skull larger, but the dura mater was not injured. With regard to Mr. Mollison's case, Mr. Tod did not advise anything being done at present, as the wound was still somewhat septic.

The PRESIDENT remarked that it had been said that if there was a hernia owing to a hole in the skull, the best way to get rid of it was to make the hole larger. This probably conveyed a germ of truth, for a decompression operation in another part of the skull would relieve it if there were symptoms. As there were no symptoms in the present case it was scarcely worth while to run the risks of trauma which an operation might involve.

## Otological Section.

November 15, 1912.

Dr. J. DUNDAS GRANT, President of the Section, in the Chair.

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### Two Cases of Vertigo in which the Blood-pressure was very Low and Reactionary Vertigo was Excessive after Rotation.

By RICHARD LAKE, F.R.C.S., & A. FERGUSON PENNY, F.R.C.S.I.

THE two following cases, whose notes we present before the Section, are of interest from several points of view. The main feature in both cases was the association of vertigo of a severe and distressing type with an exceedingly low blood-pressure. In the second case, the attacks of vertigo were so frequent as totally to incapacitate the patient. Even a slight movement of the head to one side or the other was sufficient to provoke an attack which, in every instance, was accompanied with a feeling of nausea. The administration of ernutin with the object of raising the blood-pressure proved eminently satisfactory in both cases. The first case was noted, and treated with ernutin, before we had seen Dr. Byrne's book, and although we had every reason to be satisfied with the action of that remedy in this particular case, we commenced the treatment of the second case with strychnine and atropine. After four days' treatment she reported that she was considerably worse, and she was then given ernutin. Her condition improved markedly and rapidly as the result of the exhibition of this remedy.

#### CASE I.

This patient, a clerk, gave his age as 55, but he looked considerably older. He had a slight deafness on both sides which began twenty years ago, and tinnitus also, most marked in the right ear, but not of

a severe type. There had never been any discharge, and beyond a slight retraction there was nothing abnormal in his drum membranes. He had for some years suffered from attacks of giddiness which, of late, were increasing in frequency. During these attacks he noticed that, as a rule, objects moved from the left to the right. He staggered at times, and found considerable difficulty in walking straight. He appeared to be a very neurotic subject.

He was examined, in the first instance, by one of us at the hospital on February 23, 1912, and by both of us at Harley Street on March 5. The results of both examinations were practically the same. On rotating him for the usual ten times in twenty seconds he got a most intense vertigo, accompanied by vomiting, at the hospital, and on each occasion he shot out of the chair, falling over to one side in a state of considerable collapse. A similar severe attack of vertigo followed syringing with cold water in the form of a caloric test. We found his blood-pressure exceedingly low; after rotation it was only 105. He was treated with  $\frac{1}{2}$  dr. doses of ernutin thrice daily by Dr. James, of Ealing, with the object of raising his blood-pressure. Since this treatment was adopted he has had no further attacks of vertigo. The doses were gradually reduced, and on April 4 Dr. James reported that he was quite well.

#### CASE II.

This patient, a female, aged 49, was first seen on March 8, 1912. She stated that her deafness began eight years ago in both ears, accompanied with tinnitus, and that the latter was worse on the right side. There had never been any discharge. She had paracusis Willisii. Her first attack of vertigo came on three years ago. The attacks increased in frequency, and when she came to the hospital she could not walk straight unless she fixed her eyes on the object she was approaching. Any deviation of the head or eyes to the right or left immediately brought on an attack of vertigo, with a tendency to fall to the side of the deviation, the tendency in most instances, however, being to fall to the right. The vertigo was always accompanied by a feeling of nausea, objects appearing to move in a horizontal plane from right to left. Turning over in bed produced the same phenomena. She fell two years ago during an attack. She complained of pain in the occipital region, spreading to the side of the neck and chest. She has double cataract.

Patient's present condition (May 2, 1910): She can walk straight only when the head is fixed. Turning the head or body produces vertigo and nausea, with movements of objects from right to left and a tendency to fall to the right if the movement is towards the right, and towards the left if the movement is towards the left. With the eyes closed and seated upright on a chair, when the head was turned either to the right or left, vertigo and nausea were produced.

April 17, 1912: Rotation ten times in twenty seconds resulted in an excessive reaction—i.e., excessive vertigo, nausea and nystagmus, whichever way she was turned. The patient had to be supported, as otherwise she would have fallen to the side of rotation. Blood-pressure: After rotation clockwise the blood-pressure was 95; after rotation counter-clockwise the blood-pressure was 105. Irrigation, with 8 oz. of cold water in each ear, gave slight nystagmus only.

On May 16 the patient was put on strychnine and atropine (liq. strych. 5 minims, liq. atrop. 1 minim).

On May 20 patient reported that the above mixture made her much worse. She staggered considerably, got frequent attacks of vertigo and nausea, and had one especially severe attack of vertigo, succeeded by vomiting. Her condition on May 20 was as follows: (1) The tinnitus in both ears, especially the right ear, much worse; but she did not notice any increase in deafness. (2) Her hands get cold and white, and her fingers swell. She has pains in her arms, hands and occiput. (3) Stoop-ing with the head down produces an immediate attack of vertigo and nausea, but sitting upright relieves both, and leaning with the head back increases both. A strong light on her eyes also causes an attack. On dull, cloudy days she finds that she does not suffer so much from vertigo. A loud noise brings on an attack. Blowing the nose forcibly relieves the vertigo and nausea.

To-day (June 20) the strychnine and atropine mixture was discontinued, and she was put on ernutin,  $\frac{1}{2}$  dr., t.d.s.

On June 27, after taking ernutin for two days only, she reported as follows: (1) She is much less giddy and can walk more steadily. (2) She perceived a marked difference after she had taken three doses of the ernutin, and found she could walk without staggering or vertigo. On testing her with rapid side-to-side movements of the head only slight vertigo and slight feelings of nausea resulted—in marked contrast to the intense vertigo and nausea produced before by this movement. Bending down with the head between the knees and then raising the head into the upright position was not productive

of vertigo and nausea. This movement previously produced the most intense form of nausea and vertigo.

July 4: Improving rapidly. Can walk comfortably without staggering. Rapid side-to-side movements of head produce only very slight vertigo and nausea. Same result from lowering head and raising it to upright position.

July 11: Last week she had no ernutin, and to-day she reports that the nausea, vertigo and staggering are much worse.

July 18: Much better again since taking the ernutin.

July 25: Still improving.

August 1: Still improving.

August 22: Much better. Can walk without staggering. Has not had an attack of vertigo for three weeks.

August 29: Walks with comfort. No nausea or vertigo. Feels generally much better.

September 26: No vertigo for five weeks.

P.S.—Patient's nervous system was examined by Dr. Grainger Stuart, who reported that there was no nerve disease.

#### DISCUSSION.

Mr. LAKE added that the suggestion regarding ernutin came from Mr. Penny.

Mr. C. E. WEST asked what the blood-pressure stood at before the rotation in Case I, and whether the patient was nauseated in any way.

Dr. MILLIGAN thought the exhibitors were to be congratulated on the results, but he would like to hear whether either of them could give any explanation of why the blood-pressure was so low. Was there anything wrong with the capillary system, or was there any vasomotor disturbance?

The PRESIDENT (Dr. J. Dundas Grant) asked what the tuning-fork tests indicated in regard to the localization of the trouble, and the nature of the change which caused the dullness of the hearing. These cases of low pulsation were probably of the same class as those to which Dr. Randall, of Philadelphia, drew attention at the meeting of the International Congress, and in which he had administered adrenalin or powdered suprarenal gland. This no doubt raised the blood-pressure, and acted somewhat in the same way as ernutin.

Dr. H. J. DAVIS referred, in this connexion, to his own case (*see* p. 33). After reading the notes of this case, he had given his patient  $\frac{1}{2}$  dr. of ernutin three times a day. This was four days ago, and the patient had not had an



attack since. He had not ascertained the blood-pressure, but nothing he had previously given her did good.<sup>1</sup>

Dr. DAN MCKENZIE said it was well known that any considerable alteration of blood-pressure caused vertigo, and if one gave adrenalin in a case of high blood-pressure the result might be disastrous.

Mr. LAKE replied that he did not remember that there had been any nausea. He had never tried adrenalin in these cases; he believed it lowered the blood-pressure, except for a short time.

Mr. PENNY replied that it was difficult to determine what was the cause of the low blood-pressure. He had the cases carefully examined by a physician, but could get no information on the point. The effect of the ernutin was most marked, especially in the second case. After taking the drug there was a definite rise in the blood-pressure.

### Case of Aberrant Carotids.

By RICHARD LAKE, F.R.C.S.

A WOMAN, aged 60. On each side of the lateral wall of the pharynx a pulsating vessel is visible. The exhibitor is of opinion that these are the internal carotid arteries.

### DISCUSSION.

Dr. H. J. DAVIS said that a well-known specialist in Chicago had lately described to him how, when demonstrating to a class how to open a quinsy, he found himself covered with blood, the explanation of which was that he had opened an unsuspected aneurysm of the internal carotid. He tied it, and the patient eventually was not much the worse.

Mr. ROBERTS WOODS (Dublin) said that during the last two months he had seen such a case as Dr. Davis mentioned. It was that of a married woman who had all the appearance of having a supratonsillar abscess. Her doctor, recognizing there was something unusual about it, made a cautious incision with a fine tenotome, and was met with a very forcible spout of blood. No further trouble ensued; the condition was one of aneurysm, for which the common carotid was successfully tied by Mr. T. E. Gordon; on the other side the carotid artery was normal.

<sup>1</sup> November 27: The patient has had one attack of vertigo in three weeks since taking ernutin.—H. J. D.

Mr. JENKINS said there was a complete account of such aberrant internal carotids in anatomical works; it was said to be more common in old age than in young people. Sometimes aberrant internal carotids went downwards and forwards in relation to the lateral wall of the pharynx in young subjects.

Dr. MILLIGAN questioned whether the aberrant artery was not the ascending pharyngeal. In every operation for the removal of adenoids he taught his students to examine carefully the posterior pharyngeal wall for tortuous vessels.

Dr. SALISBURY related an experience in the practice of a Leeds surgeon similar to that spoken of by Dr. Davis. There was an aneurysm of the carotid, which vessel was out of place, and there was a peritonsillar abscess in front of the aneurysm.

Dr. WATSON-WILLIAMS said it had been found that such abnormally large pulsating vessels on the posterior pharyngeal wall proved to be the ascending pharyngeal artery, though usually they were internal carotid arteries. They were more frequent than generally believed, but he had continually urged that as a matter of routine before the adenoid operation the operator should look at the back of the pharynx to make sure there were no aberrant vessels. In that way a possible disaster would be avoided; nevertheless it seemed likely that fortunately, when the operation for adenoids was done in the usual routine way, such vessels might escape.

Mr. LAKE, in reply, said that the first case of the kind he knew was recorded by Dr. Brown Kelly, in the *Glasgow Journal of Laryngology*.

### **A Method of making a Periosteo-meatal Flap in the Radical and Modified Radical Mastoid Operations.**

By HUGH E. JONES.

HITHERTO all the flaps described for these operations have involved severing the periosteum at the meatal margin, while the cutaneous flap retained a base attached to the conchal skin. One objection to a flap of this kind is that the soft parts of the meatus have to be crushed and dragged forwards and outwards during the operation; and another, that some of the periosteum is usually lost. In the method about to be described the skin-flap is completely severed from the surrounding skin, but retains its attachment to the periosteum, which is reflected upwards and backwards through the post-aural incision—to be replaced, on the completion of the bone operation, on the posterior wall of the bone cavity.

The steps of the operation are, briefly:—

(1) Make an incision through skin in the hair line behind the ear, curving upwards opposite the highest point of the ear into the scalp for about  $\frac{1}{2}$  in. (Ballance's incision). (Fig. 1, *s, s'*.)

(2) Reflect the auricle forwards until the meatal edge can be defined, leaving the periosteum and meatus uninjured. (Fig. 2, *b*.)

(3) Make two nearly parallel curved incisions through the periosteum from the upper and lower margins respectively of the meatus nearly to the posterior border of the mastoid bone. (Fig. 2, *p p, p' p'*.)

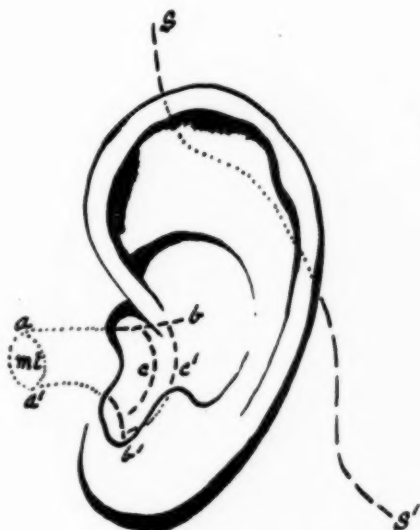


FIG. 1.

(4) Separate the outlined periosteal flap from the outer surface of the mastoid and well into the osseous meatus.

(5) Replace the auricle, and make two incisions through the soft parts of the meatus from the tympanic ring outwards—one at the highest, and the other at the lowest, point of the meatus. (Fig. 1, *a b, a' b'*.)

(6) Cut through the base of the posterior meatal flap at the point in or near the conchal margin, which is judged to give a sufficiently enlarged meatus. (Fig. 1, *c* or *c'*, *c* preferred.)

(7) A few touches with the scissors or scalpel will now enable the

operator to lift out the posterior wall of the membranous and cartilaginous meatus and the periosteal flap, in one piece. (Fig. 3, *Pf*, *Mf*.) The combined flap is turned backwards and protected by gauze until the bone operation is completed. Finally pass a strip of gauze, linen, or india-rubber of suitable width through the posterior meatal incision, and hold forward the auricle and post-aural skin-flap. (Fig. 3.)

By this method, as soon as the flap is completed and the hæmorrhage arrested, an excellent view of the meatus is obtained and, if this

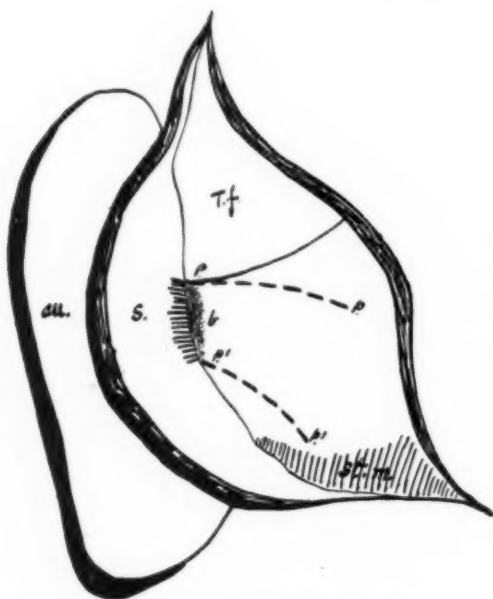


FIG. 2.

is free from granulations and débris, of the membrana tympana or the tympanum itself. The meatal tissues do not suffer during the operation, and the anterior half is undisturbed. The flap retains the whole of the periosteum, and helps to fill up the bone cavity. The skin surface has more growing edges than the ordinary flap, and should therefore give greater assistance in epithelializing the cavity.

The method is applicable to all *primary* radical or modified radical mastoid operations, but is obviously not suitable for cases in which there has been extensive separation of the periosteum and an external

fistula. Where subsequent secondary operations extending intracranially are likely to be required, the flap described would not cause any serious inconvenience, but is not recommended. Where it is desirable to remove the mastoid cortex down to the tip, the lower periosteal incision should curve sharply downwards near the anterior border of the mastoid process.

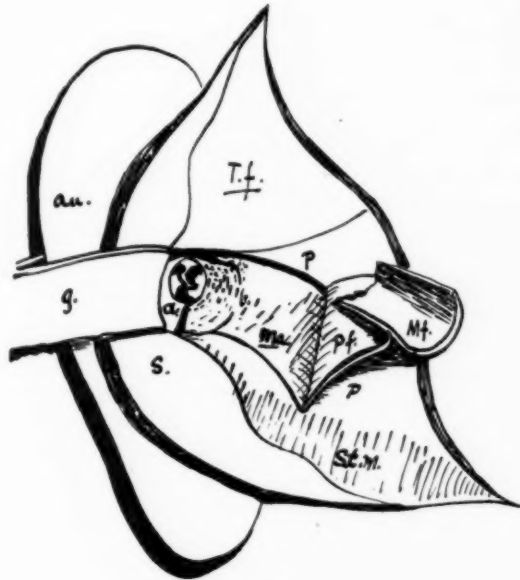


FIG. 3.

### DISCUSSION.

The PRESIDENT said that Mr. Jones had described what was to him a novel form of plastic flap. He presumed there was sufficient nutrition for the comparatively thicker skin from the thinner periosteum. He asked if Mr. Jones had observed any sloughing of tissue in the flap afterwards.

Mr. HEATH said that the fact that Mr. Jones had brought this flap to the notice of the Section showed that he had not been satisfied with the flaps which had previously been in vogue. With regard to the utilization of the whole of the posterior half of the cartilaginous meatus as the covering of the cavity, he had utilized it, separate from the pericranium, for five or six years, and did so in acute and chronic cases, and in conservative and radical operations.

With regard to the pericranial flap, he had used a shorter one than that described by Mr. Jones, because he made his incision so much nearer the ear. He had used the meatal flap for twelve years, and the pericranial one for six years. The advantage of having them thus separate was, that if there was too much of one flap they could be more or less overlapped, and thus it did not matter much, as he always stitched them together. He found the method so satisfactory that he saw no reason to change it. His own skin incision was made immediately behind the ear, and therefore the pericranial flap was necessarily much shorter than the one now advocated by Mr. Jones. With regard to the advantage of having the whole meatus visible during the operation, he was not sure it was an advantage; he preferred to have the tympanic parts protected by a retractor which pressed against the posterior wall of the meatus, deep in, so that there was no chance of an instrument reaching the drum-head by accident. The removal of the posterior half of the cartilaginous meatus enabled the surgeon to see the tympanic area, and for that reason he had temporarily removed it in every case for six years. He had abandoned Schwartze's operation for that number of years. The great point about having a single meatal flap was, that it could be put at the back of the antral cavity, out of the way. Because if one turned a piece up it swelled and hid the antrum, and if turned down swelled and hid the tympanum, and it was desirable that those parts should be visible during the after-treatment.

Mr. C. A. BALLANCE remarked that ever since otologists made a flap of the membranous meatus the otologist had dealt with the posterior wall of the membranous meatus. One knew many methods of dealing with the posterior wall of the membranous meatus, and Mr. Jones had now brought forward a new method, which he (Mr. Ballance) believed would develop into an admirable one. He felt immensely indebted to Mr. Jones for having introduced it, and he intended to try it himself.

Mr. BADGEROW regarded the method as a very good one, and said he had used practically the same flap, except for the skin incision. Mr. Jones went back into the hair, and then made a periosteal flap; he had seen Mr. Heath when at Golden Square use practically the same meatal and pericranial flap in all his cases for the last six years.

Dr. WATSON-WILLIAMS said he gathered that one new feature in this very promising and suggestive flap was, that the posterior meatal wall skin-flap was completely detached from the skin all round, and that "the one string to its bow" was its attachment to periosteum. He did not gather that other flaps just referred to by Mr. Heath and Mr. Badgerow were thus completely isolated, and as far as he could understand their remarks, Mr. Hugh Jones's flap was quite a different thing.

Mr. HUGH JONES replied that until the day before he did not know Mr. Heath made a periosteal flap, but he now saw that the periosteal part of Mr. Heath's flap was something like what he had himself now described. But in the flap demonstrated the meatal skin and periosteum remained unsepa-

rated; the essential difference was that, in the method now described, the periosteo-meatal flap was cut in one piece at the beginning of the operation, so as to give a clear view of the osseous meatus and tympanum. The nourishment of the flap was the one fear he had. He had not seen the nourishment fail, but he had not yet had occasion to reopen a case in which the operation had been done, so that he could not say exactly what happened to the flap eventually. It was as yet experimental, but he thought he would like to bring it forward at once, so that other surgeons might try it. He himself had employed the method twelve or fifteen times and thought it was "satisfactory."

### **Thrombosis of Jugular Bulb; Ligation; Empyema; Recovery.**

By C. ERNEST WEST, F.R.C.S.

L. M., FEMALE, aged 20. History of left otorrhœa for three weeks, pain behind ear five days, swelling four days. No history of sickness or giddiness. Doubtful history of two rigors on day of admission. Headache; no pain in neck. Admitted on June 3, 1912, to St. Bartholomew's Hospital. Temperature on admission, 102·4° F. Pulse 108; respiration 24. The posterior wall of the meatus was prolapsed, obscuring the view of the membrane. Edema and redness but no fluctuation over the mastoid. Great tenderness, especially towards tip of process. Glands along jugular not felt to be enlarged. Pupils equal; no nystagmus.

A Schwartze operation was carried out immediately. The lateral sinus was exposed in the course of the operation and appeared normal. A Bezold's perforation had taken place through the tip of the mastoid. Temperature subsequently remained of an oscillating type, with a rigor on two occasions.

Second operation (June 13): The sinus was examined and found healthy in the exposed portion. On following it downwards the jugular bulb was found thrombosed and its wall necrosed. The vein was tied in the neck and the bulb cleared out.

Subsequent history: Great improvement for three weeks as regards temperature, but failure to improve in general condition; then renewed rise of temperature. After two explorations empyema found low down on left side: opened and drained (1½ pints). This was followed by some subdiaphragmatic peritonitis. Final complete recovery.

Bacteriology: From the jugular bulb were grown streptococci and a Gram-negative bacillus. From the empyema were grown streptococci and a diphtheroid organism.



### **Injury to Internal Carotid Artery in Curetting Tympanic Part of Eustachian Tube.**

By C. ERNEST WEST, F.R.C.S.

J. M., FEMALE. Chronic suppurative otitis media, right. Radical mastoid operation (July 9, 1912): Upper part of Eustachian tube curetted out. In finally withdrawing curette, injury to internal carotid. Hæmorrhage controlled by digital pressure in neck. Immediate ligation of common carotid. No further hæmorrhage. Uninterrupted recovery.

#### **DISCUSSION.**

Mr. WEST apologized for the absence of both his cases. They were both in service at considerable distances, and he had not felt justified in bringing them to show their healed scars. He had reported the first case because it had several points of rarity; it was a case of thrombosis in a recent otitis media; the thrombosis was primary in the jugular bulb, and the patient recovered after a serious pyæmic complication in the thorax. It was the first case which he had had in which the patient got finally well after such invasion of the lung and pleura. He gave the credit to his house surgeon who had fought for success in magnificent style. In the second case he did not know why the carotid was injured; he was not using any undue violence or pressure in curetting the tube, and he supposed that there had been a hiatus in its inner wall. There had been no apparent ill-effects from the unfortunate accident. He believed ligation of the carotid was the only possible treatment of the condition if the patient's life were to be saved. In this case the alarming feature had been not the total amount of blood lost but the great violence of the hæmorrhage while it lasted. The patient was in the early twenties, and that might have something to do with the completeness of her recovery.

Dr. MILLIGAN agreed that such cases were rare, but not excessively so in children. He supposed very few members had seen recovery after septic pneumonia or empyema secondary to sinus thrombosis. He did not think so many thrombotic cases were seen nowadays as ten years ago, and the explanation probably was that more attention was now paid to the early treatment of ear disease. He had had a similar misfortune to that detailed in the second case, in a patient aged 60, the operation being a complete labyrinthectomy. He discussed with the medical man in attendance the various ways of sealing

up the Eustachian tube, and remarked how difficult it was to be certain that it had been effectively closed. In this instance he used a burr with the ordinary care. In a moment there was a swish, and the wound was filled with blood. He put his finger into the bottom of the wound, and rapidly plugged it. He packed it very tightly, and in twenty-four hours he gently removed the packing, with the aid of hydrogen peroxide, and again there was severe hæmorrhage. He decided not to tie the carotid, but plugged again, and there was no further hæmorrhage. The force seemed to be too great for it to be venous blood. The patient was fairly deeply under continuous ether anaesthesia. The vessel from which the bleeding came must have been an aberrant one. He asked whether Mr. West could prove that the hæmorrhage in his case was carotid artery bleeding, not from an aberrant jugular bulb.

Mr. HUGH JONES said the only case he had seen in life of primary thrombosis of the bulb was caused by himself in curetting the floor of the tympanum. He had been using chromic acid on account of granulations growing from the floor of the tympanum, and thrombosis of the bulb ensued. The man recovered after ligation of the jugular vein.

Mr. JENKINS said he thought it would be well if Mr. West would give the meeting the explanation he gave at the demonstration of the case of why he tied the common carotid and not the internal. The difficulty of tying the latter was great, but sometimes it was less than tying the external. It was yet early to know whether there had been serious effects from the ligation. Ill-results might ensue six or nine months afterwards.

The PRESIDENT, referring to thrombosis of the jugular bulb, said that years ago Leutert wrote a long paper showing that in children with acute suppuration in the middle ear, if the temperature was high and there was vomiting for a few days, there was some thrombosis of the bulb, usually of the parietal form. This might disappear altogether, but Leutert recommended operation.

Mr. WEST replied that he did not of course see that it was the internal carotid which bled, but he could not conceive of the jugular bulb being where his curette was when the bleeding began, and he had never seen a venous channel approach the fury with which this bled. Further, the bleeding was immediately controlled by pressure over the carotid. The hæmorrhage down the Eustachian tube was very severe, and he could not control it at all by packing the tympanum. There seemed no room to him for doubt that the bleeding came from the carotid. He tied the common carotid because there was inadequate room to get at the internal carotid when two fingers were being employed to compress that vessel. He attempted what he could do most quickly.

**Cerebellar Hernia following Cerebellar Abscess in a Boy,  
aged 8.**

By H. J. DAVIS, M.B.

At the first operation on May 20, 1912, in addition to an acute mastoid abscess being opened, a large extradural abscess in the posterior fossa was dealt with in the usual way. The boy was very ill, but made



Cerebellar hernia : Appearance in June, 1912, three weeks after evacuation of large cerebellar abscess.



Appearance in September, 1912, when the hernia had receded and skinned over and was flush with the head.

a good recovery. On June 10, three weeks later, he became sick and drowsy, and developed optic neuritis with nystagmus to the opposite side. I operated on him the same evening and evacuated a large abscess in the right cerebellar lobe containing 2 oz. of pus. To complicate matters the lateral sinus gave way and hæmorrhage was not easy to control owing to the amount of bone already removed, and to the protrusion of brain matter. The boy slowly recovered, but the hernia protruded more and more until it reached the size shown in the two photographs exhibited. When pressure was exerted by bandaging, sickness and giddiness followed. The question of shaving off the redundant tissue

was entertained but nothing was done, and, as can be now seen, the hernia, which was a very large one, has receded, skinned over, and is flush with the head. The boy is quite well.

This case is the one the exhibitor alluded to at the last meeting of the Section during the discussion on Mr. Mollison's case.<sup>1</sup>

This case is instructive from other points of view:—

(1) The jugular vein was never tied. At the Manchester meeting last June several cases of lateral sinus thrombosis were exhibited in which recovery had taken place without the usual ligation of the vein. This shows that although a septic clot exists it does not necessarily extend and cause damage, though undoubtedly it must be safer to tie the jugular as an extra precaution.

(2) Did the abscess originate by direct infection along the track of the first exploration into the cerebellum? This was done with a fine knife and every care taken to prevent infection, but the possibility of this occurring is a very important consideration when pus is spread over the outer surface of the dura mater. It is the practice of the exhibitor not to explore the brain in perisinus suppuration if the brain is pulsating, unless, as in this case, there are other reasons to the contrary.

Report of pus organism: (a) Films—a few Gram-positive diphtheroid bacilli; (b) cultures—the same organism grown on serum and agar.

#### DISCUSSION.

Mr. MOLLISON described the sequel to the case of cerebral hernia which he exhibited at the last meeting. The night following the meeting the boy woke up screaming, he was sick occasionally; two days later optic neuritis was present, while previously an expert had found the disks clear. In consultation, a physician agreed there must be some pus in the cranium, probably in the cerebellum, as abscess in the site of a previous cerebral abscess was rare. Operation: Exploration of cerebellum with a narrow knife revealed nothing, neither internal to nor posterior to the lateral sinus. He covered that site with gauze, and explored the position of the old cerebral hernia; with forceps he penetrated the thick capsule of an abscess, and let out 2 oz. of very fetid and thick pus, which he felt sure had been there weeks. The cavity, which extended forwards into the frontal lobe, was washed out and a double drainage-tube inserted. Three days later, while being dressed, the boy stopped breathing, but artificial respiration for ten minutes brought him round. Further exploration revealed no further collection of pus, and he was now much better, there was less vomiting, and he was taking food well. Right hemiplegia and aphasia developed, due probably to thrombosis

<sup>1</sup> *Proceedings*, p. 15.

of the left middle cerebral artery, so that even if he recovered, his position would be very parlous. No doubt this abscess had been present many weeks and accounted for the hernia. The case showed very beautifully the importance of the superficial abdominal reflex. Two days before operation the right abdominal reflex was much less than the left, and it disappeared the day of operation. Next morning it was present again, and normal. It would be remembered that the importance of the superficial reflexes was emphasized by Sir Victor Horsley in a paper he read before the Section in January, 1912.<sup>1</sup> Another point of interest lay in the fact that though the pus from the abscess flowed over the two exploratory incisions in the cerebellar dura mater no infection followed.

Dr. MILLIGAN said that in such cases the first thing to do was lumbar puncture; it relieved intracranial tension, and probably prevented sudden respiratory paralysis, which was common in cerebellar abscess. These hernias sometimes contained fluid, even pus. He had seen a hernia of the same size containing glairy fluid, possibly from broken-down necrotic brain tissue. It was justifiable to put an aspirator into such hernias. Failing getting anything away, one might keep up continuous lumbar drainage for days, or even weeks. That failing, one could perform a decompression operation.

Mr. JENKINS corroborated what Mr. Mollison said as to the importance of the abdominal reflex. He had a case of meningitis, localized to the left cerebrum, and the right abdominal reflex was totally abolished, the left present.

Dr. DAVIS replied that several times he had perforated the hernia with a Horsley pus-seeker, but nothing came out. The serious feature had been the position of the hernia. He had not used pressure, for when that was done the boy became sick and giddy.

[*Addendum*.—Dr. Neumann, of Vienna, asked me to record his and Ruttin's tests in this case. I have done so, and the results are as follows:—

- (1) Is there any spontaneous nystagmus?—Yes; rotatory to the left.
- (2) Result of pressure on the hernia.—Rotatory nystagmus to the left is increased.
- (3) Syringing the diseased ear with cold water.—Yes, nystagmus to the left.
- (4) During syringing, does pressure on the hernia alter the direction of or the intensity of the nystagmus?—Yes, it increases the intensity of the nystagmus to the left.
- (5) Syringe the sound side (cold water) for one minute; how long does the nystagmus last?—Horizontal nystagmus to the right for two minutes.
- (6) Repeat this again on another day: does the pressure on the hernia alter the character of the nystagmus?—Yes, the horizontal nystagmus to the right is arrested by pressure on the hernia.

<sup>1</sup> *Proceedings*, 1912, v, p. 49.

(7) Try Bárány's pointing test with the finger: is there any deviation or not? (a) "Up and down?"—Yes, to the right. (b) "Side to side?"—Accurate.

(8) Does pressure on application of ice to the cerebellar prolapse alter the accuracy of the pointing? (a) "Up and down?"—Yes, increases the inaccuracy to the right. (b) "Side to side?"—Accurate, no change.

(9) Try the same experiment with both feet. (a) "Up and down?"—Yes, to the right. (b) "Side to side?"—No change.—H. J. D.]

### Labyrinthine Vertigo; (?) Auditory Tumour; Woman, aged 33.

By H. J. DAVIS, M.B.

MRS. M., aged 33, was admitted to the medical wards under the care of my colleague Dr. Saunders, for violent attacks of giddiness, lasting from two to twelve hours. Medically, nothing could be found to account for this, and as symptoms pointed to the labyrinth as the cause I was asked to see her. The patient has no children, and she has never menstruated. Briefly, she hears nothing in the right ear, though she seemed quite unaware of this. The left ear is normal, and when occluded by Bárány's apparatus the patient is quite lost; in other words, the cochlear nerve is functionless, and the vestibular nerve nearly so, for the only reaction obtained is ten minutes after syringing with ice-cold water. There is slow nystagmus on looking to the right and not to the left, as would be expected. The patient, a very intelligent woman, says she is quite well but for these attacks, which commenced in a small way two years ago, but the last few months they have been much worse. She was advised that the attacks were "biliousness," and she was told to take no notice of them, but this was not an easy thing to do, for she dropped in the street like a log, and her friends thought she was dead.

The exhibitor is of opinion that the disease is due to an implication of the auditory nerve before it enters the internal ear, and that this is probably due to a tumour.

Wassermann test negative.

[*Addendum*.—December 15, 1912: Since this patient has been treated by ernutin (30 minims, thrice daily), as recommended by Mr. Lake, she has had only two attacks of vertigo in five weeks and the blood-pressure, which was low (118), has been raised to 130 with great and rapid movement.—H. J. D.]

### **Malignant Polypus of the Ear.**

By H. J. DAVIS, M.B.

MAN, aged 56, with an aural polypus; six weeks' history. This was snared and removed with a curette. The polypus is malignant; no other signs yet. A microscopical section was exhibited, showing malignant growth, and, as pointed out by Mr. Ballance, resembling scirrhus.

[*Addendum*.—December 15, 1912: Three days after the patient was exhibited I performed a radical mastoid operation. The middle ear was found to be full of friable growth which kept bulging into the tympanum as fast as it was removed. It was eventually seen that the roof of the tympanum had been invaded by the growth which had extended and implicated the dura mater on the under surface of the temporo-sphenoidal lobe. This was curetted away and so far the patient is quite comfortable and the wound has healed, but the patient has lost his memory and is very irritable, though he is up and about the ward.—H. J. D.]

### **Acute Middle-ear Suppuration; (?) Cavernous Sinus Thrombosis; Recovery.**

By DAN MCKENZIE, M.D.

FEMALE, aged 11, a puny and delicate child. A week previous to my seeing her acute suppuration of the middle ear set in with high temperatures. A few days later proptosis of the right eye was observed. There was some drowsiness, and the patient had vomited once. When I first saw her there was marked protrusion of the right eyeball, chemosis and œdema of the eyelids. The pupil reacted, and there was no evidence of paralysis. Examination of the fundus, made by Dr. Salisbury a few days later, revealed some venous distension.

Immediate mastoid operation, radical, in view of the apparently serious intracranial disease. Lateral sinus exposed, slit up, and found to be normal. After the operation temperatures ranged between 98° and 101° F. for ten days and then became normal. The eye was less prominent forty-eight hours after operation, and regained its normal appearance in about a week. Some suspicion of œdema was observed in the left eyelid at the operation.



The diagnosis of cavernous sinus thrombosis is, of course, problematical. Mild venous infection with thrombosis and recovery occurs elsewhere in the body, even in the lateral sinus, it is said. Thus there is no inherent impossibility in the same series of changes affecting the cavernous sinus.

I am indebted to Dr. Salisbury, Resident Medical Officer, Central London District Schools, Hanwell, for permission to show the case and for the notes upon it.

#### DISCUSSION.

The PRESIDENT thought the diagnosis more probable than problematical, but it might not have been an infective thrombosis. Still, he thought there was a clot, or at all events some obstruction to the return of blood.

Dr. MCKENZIE replied that he had some hesitation in putting that name to it, but aseptic thrombosis of veins occurred elsewhere, and the symptoms were the same as those of cavernous sinus thrombosis. Both ears were the seats of acute suppuration, and there was some doubt as to which ear should be operated upon; but the ear was chosen which was on the same side as the proptosis.

#### Lens for Use in Mastoid Operations.

By DAN MCKENZIE, M.D.

THE lens is mounted on a detachable and sterilizable rim and handle. It is useful in examining the outer labyrinth wall.

Mr. HUGH JONES said he used a pair of +5' lenses (cut from one large lens) fitted on to a headlamp frame, which he found very handy. The frame was an open one, like a trial-frame, and other lenses of different strength could be substituted. The lenses were cut square so that the correct prism effect could always be got when they were inserted into the frame.

## Two Cases of Operation for Chronic Adhesive Catarrh of the Middle Ear (Tympanoplasty).

By H. A. KISCH, F.R.C.S.

*Case I.*—S. McK., boy, aged 15; deaf for years in both ears. No throat or nose trouble. Not improved by catheter treatment. Membrane very retracted; malleus slightly movable. Paracusis Willisii present. Operation was performed in January, 1912, on the right ear. The tympanic membrane, the malleus incus, and all the mucous membrane of the middle ear were removed through a retro-auricular incision. A foramen was gouged in the promontory and the cavity then grafted. The stapes was fixed. After-treatment by massage was carried out, and for the last two months ionization with salicylate has been used. Hearing tests, before and after operation:—

| <i>Before (January 15, 1912).</i> |                |       |                 |     | <i>After (October 31, 1912).</i> |                |        |                 |     |
|-----------------------------------|----------------|-------|-----------------|-----|----------------------------------|----------------|--------|-----------------|-----|
|                                   | Air-conduction |       | Bone-conduction |     |                                  | Air-conduction |        | Bone-conduction |     |
| C <sub>128</sub> ...              | -120           | ...   | +11             | ... | C <sub>128</sub> ...             | -22            | ...    | +7              | ... |
| C <sub>256</sub> ...              | -56            | ...   | +12             | ... | C <sub>256</sub> ...             | -80            | ...    | +3              | ... |
| Whisper ...                       | ...            | 1 ft. | ...             | ... | Whisper ...                      | ...            | 9 in.  | ...             | ... |
| Voice ...                         | ...            | 9 in. | ...             | ... | Voice ...                        | ...            | 6½ ft. | ...             | ... |

*Case II.*—M. T., girl, aged 19; deaf for years. No improvement on treatment. Has slight hypertrophic rhinitis. Membrane retracted and slightly movable. Paracusis Willisii present. A similar operation to that of the previous case was performed in January, 1912. The stapes was fixed. Patient had severe headaches afterwards, which subsided later. The hearing was improved immediately after operation, but relapsed six weeks later, the patient becoming totally deaf and suffering from severe tinnitus. This did not improve, and a second operation was undertaken. The skin-graft was removed; the foramen in the promontory was apparently filled up with fibrous tissue. A fresh graft was inserted. After this the hearing improved. There has been one rather severe relapse with subsequent recovery. Similar after-treatment to the previous case has been used. Hearing tests before and after operation:—

| <i>Before (December 2, 1911).</i> |                |        |                 |     | <i>After (October 31, 1912).</i> |                |        |                 |     |
|-----------------------------------|----------------|--------|-----------------|-----|----------------------------------|----------------|--------|-----------------|-----|
|                                   | Air-conduction |        | Bone-conduction |     |                                  | Air-conduction |        | Bone-conduction |     |
| C <sub>128</sub> ...              | Not heard      | ...    | +10             | ... | C <sub>128</sub> ...             | -30            | ...    | +9              | ... |
| C <sub>256</sub> ...              | -55            | ...    | +4              | ... | C <sub>256</sub> ...             | -54            | ...    | +15             | ... |
| Whisper ...                       | ...            | 4 in.  | ...             | ... | Whisper ...                      | ...            | 5 in.  | ...             | ... |
| Voice ...                         | ...            | 10 in. | ...             | ... | Voice ...                        | ...            | 5½ ft. | ...             | ... |

## DISCUSSION.

Mr. LAKE pointed out the need for using some definite formulæ for ear testing in order properly to be able to ascertain the value of these operations. Tests were of great importance if one could look at them through, as it were, one's own spectacles.

Mr. JENKINS asked whether the case was considered to be one of otosclerosis, as the patients had paracusis. Also, how did Mr. Kisch estimate the paracusis? Did he take the word of the patient for it, or had he other means of arriving at it?

Mr. MOLLISON asked, in regard to the second patient, what permanence there was likely to be, as he could not make her hear conversation at 2 in. that afternoon. If such cases were going to improve as the first one did, the operation might well become very frequent.

The PRESIDENT said the gross evidence given by the patients seemed satisfying and encouraging. With regard to uniformity of tests for hearing, he had proposed during last session that there should be a small sub-committee to draw up a formula somewhat like those in use on the Continent. It was an important matter, and perhaps the Council would consider it.

Dr. URBAN PRITCHARD said he thought these cases had been brought forward at the wrong time; if they could be seen in two months' time one could judge better. His testing when the room was quiet did not bring out such a favourable result as the notes indicated. One ear was still suppurating.

Mr. MUECKE said that one of the cases was no longer dry, but suppurative catarrh. It was well known that the majority of such cases heard better when the ear was discharging than when dry; could not this account for the small increase of hearing?

Mr. KISCH replied that the suppuration in the ear was due to the use of ionization, as before this was used the ears were dry. The discharge came from the posterior wall of the meatus. He agreed with Mr. Lake about the tests. Both the patients had given practical evidence of improvement; the boy had got work since he could hear, and the girl could hear the bells in the house. These cases varied from day to day, but 2 in. was less hearing than was the actual. They were not true otosclerosis, as the stapes was not fixed by bone. In a case of Dr. McKenzie's the stapes was fixed by bone, and the sensation imparted on probing was different. It was important to ascertain beforehand whether it would be necessary to open the promontory, as it greatly increased the risk of the operation. He had used the increase of bone-conduction as the guide; the greater the bone-conduction the more fixed was the stapes. He took the patient's word for the paracusis.

**Chronic Diffuse Labyrinthitis in a Man, aged 58. Horizontal Canal drained by a Strand of Silkworm Gut inserted into the Canal and buried extradurally.**

By E. A. PETERS, M.D.

G. H., UPHOLSTERER, was transferred to my department at the Bolingbroke Hospital by Dr. Lakin. The patient (February 13) complained of the Ménière syndrome—vertigo, sickness, deafness, and faintness.

Since 18 years of age he has experienced attacks of sickness of a migrainal type, which have been less pronounced the last two years, but have been accompanied by a tendency to fall backwards and a waterfall noise in the left ear. The deafness has progressed insidiously and the patient is unconscious of an increase of deafness with each attack. The vertigo, often associated with pain referred to the side of the head, has increased, and the patient is often unable to work or even go about alone. Hearing tests:—

|                                   | Right ear | Left ear |
|-----------------------------------|-----------|----------|
| Stop-watch ... ..                 | 12/60     | M3/60    |
| Tuning fork 128 on mastoid ... .. | -9 sec.   | -9 sec.  |

In the rotating chair the patient experienced no giddiness, and nystagmus was either absent or irregular, as if the function of the canals had been affected. He could turn round when the eyes were shut without inconvenience. The results of caloric tests were similar to those obtained by rotation. For ten weeks he was medically treated with diminished fluids, calomel and potassium iodide, without improvement; the attacks became more violent in character and at times he was unable to cross his dwelling-room.

On May 2 Mr. Wilson administered ether and chloroform at the Royal Ear Hospital for forty minutes. Neumann's or the posterior route to the canal was taken, and the antrum opened without disturbing the deeper lining of the external auditory meatus or the middle ear. The horizontal canal was uncapped for 1 mm., and the dura mater exposed anterior to the lateral sinus. A medium strand of rigid silkworm gut was selected and inserted into the canal 4 mm., while the other end was bent about 25 mm. beneath the dura. Grafts were applied in a cavity filled with saline, which was abstracted by suction

apparatus. The temperature was 99° F. next day, and on the third day the patient sat up for a short time, but complained of giddiness. The grafts did not take well, otherwise his convalescence was uneventful but prolonged; the dressing was continually soaked by clear fluid escaping from the opened canal.

The wound is now quite healed; the strand of gut cannot be seen, but the membrana tympani is slightly injected. His general condition has vastly improved, the nausea and giddiness diminishing daily. After the third week he sent for his tools and repaired the hospital chairs. He has now resumed his ordinary work and climbs ladders with impunity.

The hearing tests taken in September were:—

|   |  | Right ear |     | Left ear |
|---|--|-----------|-----|----------|
| Stop-watch ... ..                             |  | 14/60     | ... | Contact  |
| Speaking voice heard by the left ear at 9 ft. |  |           |     |          |
| Tuning fork 128 on mastoid ... ..             |  | - 6 sec.  | ... | - 7 sec. |
| " C <sub>1</sub> " ... ..                     |  | - 6 sec.  | "   | - 6 sec. |
| " C <sub>2</sub> " ... ..                     |  | - 3 sec.  | ... | - 5 sec. |

The rotation and caloric tests gave results similar to those observed in the first instance. I would remark that the tests suggest that the same pathological process has insidiously invaded both labyrinths, and the left labyrinth more particularly. Whether it was that particular affection of the left labyrinth which caused the vertigo and sickness, and this was relieved by the drainage instituted, or whether these symptoms were the result of the physiological interaction of two diseased labyrinths, is a matter open to doubt, and can only be cleared up by the subsequent history of the case.

Mr. JENKINS said the case was similar to one he reported some time ago, particularly in regard to nystagmus on rotation and giddiness. He drained the labyrinth by a method slightly different from that which Dr. Peters had carried out. He simply opened into the peri-lymphatic space. He did not put in silk or silkworm gut to keep up the drainage for any period. That patient was now quite well and at work, and had no attacks of giddiness. The question was still in an experimental stage and should not be approached rashly.

**Case of Osteoma of the Mastoid.**

By R. S. COCKE, F.R.C.S.

GIRL, aged 12; swelling noticed, the size of a pea, in January, 1907. Seen at the Royal Ear Hospital, February, 1908, then the size of a walnut, pressing on and partially closing the cartilaginous meatus, Removed with chisel; another growth, very much smaller, removed at the same time. Nothing noticed till eighteen months ago, when her mother saw a swelling in the same region, starting like the former, which has now grown to its present size. No pain ever; hearing normal.

Microscopical section of original growth shows typical osteoma.

**Rubber Nozzle for Syringing Backwards and Clearing out the Cul-de-sac formed by the Radical Post-aural Operation.**

By URBAN PRITCHARD, F.R.C.S.

THIS is an improvement on the similar metal nozzle shown at the meeting of the Otological Section, December 5, 1908.<sup>1</sup> Being soft, it can be introduced deeply into the meatus without producing pain. It can be fixed on to the nozzle of almost any syringe.

<sup>1</sup> *Proceedings*, 1909, ii, p. 19.

## Otological Section.

January 17, 1913.

Dr. J. DUNDAS GRANT, President of the Section, in the Chair.

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### A Discussion on the Treatment of Meningitis of Otitic Origin.

Opened by WILLIAM MILLIGAN, M.D.

OF the various intracranial complications consecutive to disease of the ear there is no one which is at times more difficult to diagnose, and, up to the present, more disappointing in its treatment than meningitis. Your Council have done me the honour of inviting me to introduce to-day a discussion upon "The Treatment of Meningitis of Otitic Origin." In acceding to their request I am fully conscious of the difficulties of the task, and can almost hear someone saying: "What is the use of a discussion upon a disease which, when diffuse and purulent, is invariably fatal?" I am optimistic enough, however, to believe that surgery which, in its triumphal march, has gained so many victories over the army of septic organisms, may, in the future, prove its ability to cope with the disease under discussion, and so add one more to its many laurels.

Despite all that has been written there is still considerable diversity of opinion as to what actually constitutes meningitis, and perhaps even greater want of unanimity as to the exact relationship between lepto-meningitis serosa so-called and lepto-meningitis purulenta. While many observers look upon the former as the forerunner of the latter, others consider the two diseases as distinct entities, while there are still others who deny the existence of any such disease as serous meningitis (Körner, Luc). That a type of otitic meningeal inflammation exists to which the name "meningitis serosa" may be fairly applied I have



personally no doubt, and that it is the forerunner of all cases of purulent meningitis is a point I hope to make in the following argument. Clinically its presence is indicated by such symptoms as headache, vomiting, stiffness of the muscles of the neck, and increase of arterial tension. Upon tapping the lumbar theca the cerebrospinal fluid spurts out under pressure; is, as a rule, clear, although it may be slightly turbid; has a specific gravity of 1005-1008, and an alkaline reaction. It may contain a few lymphocytes and polymorphonuclear leucocytes.

In the midst of such conflicting ideas it is unusually difficult to extract light from darkness, and you will, I trust, pardon me if, in the following remarks, I may appear to be didactic, and to draw too much from my own, and therefore necessarily limited, experience. The subject is one, however, which has interested me very considerably, and with the surgical treatment of which I have had some little practical experience. Considered from a pathological standpoint, it is undoubtedly convenient to divide meningitis into such subdivisions as serous, plastic, fibrinous and purulent, but from the therapeutic point of view these subdivisions are arbitrary, and are merely so many phases in the evolution of a disease, a progressive disease, the outcome of bacterial invasion, whose invariable termination, unless nipped in the bud, is in the death of the patient. I would urge the importance of this view, and of recognizing that there will always be inherent differences in the clinical landscape due to the variety and toxicity of the causal organism or organisms, and the cell resistance of the individual. That the disease is not necessarily fatal, provided that an early diagnosis be made and prompt treatment instituted, is evident from the published records of carefully observed and authentic cases. The old adage that delay is dangerous is nowhere more applicable than in the treatment of otitic meningitis. Put briefly, successful treatment depends upon early diagnosis and early drainage. Special knowledge is required in order to make an early diagnosis, and courage to operate in the absence of the full *ensemble* of text-book symptoms.

What actually determines the onset of an attack of meningitis remains as yet undetermined. Why in meningitis is there an increase, and often a very rapid increase, in the amount of cerebrospinal fluid? Why does not this increased exudate pass into the circulation, there to be dealt with? These and other such problems demand our most careful consideration. The mortality from purulent otitic meningitis is still so alarmingly high that any suggestions as to its treatment, suggestions which I trust may be thrown out in the course of to-day's

discussion, will be welcomed by all who have the progress of aural surgery at heart.

For practical purposes meningitis may be divided into two main types: (1) localized, and (2) diffuse; and into subdivisions according as it attacks the external surface of the dural or the subdural spaces.

The treatment of that localized form known as extradural abscess is so well understood by members of this Section that I do not propose to discuss it beyond remarking that, in my experience, it is a more common complication of acute than of chronic otitis media, and more frequently found in the posterior than in the middle fossa, and also that I have frequently encountered such extradural collections of pus when their existence was quite unsuspected. It is quite a different matter, however, when ulceration of the dura has taken place and infective organisms have reached the subdural spaces. It is true that localized collections of pus are found in the subdural space, but the tendency here is to generalized suppuration, as the defences thrown out by Nature are rarely strong enough to resist repeated bacterial attacks. Such localized subdural collections of pus are rarely diagnosed, but are occasionally found in the course of exploratory operation.

Purulent lepto-meningitis, by which I mean an involvement of the meshes of the pia arachnoid membrane, is by far the most formidable of the various intracranial complications secondary to purulent otitis media, and is frequently encountered with brain abscess or sinus phlebitis. For a time the infective process remains localized to the neighbourhood of the original focus of septic disease, but tends to become diffuse and generalized. The fact, however, that it remains for a time, at any rate, localized, deserves to be more appreciated, for it is at this stage that operative interference is most likely to prove successful. Exacerbations of temperature denote to my mind invasion of fresh areas of tissue, and, therefore, of an advance of the disease, and are consequently important signals. It is useless to await the advent of all the classical signs and symptoms so ably portrayed in the majority of text-books. By the time they are in evidence the patient is, as a rule, beyond the hope of surgical intervention, the increased intracranial pressure and the existing toxæmia so disorganizing his cerebral centres as to make recovery well-nigh impossible. An intelligent appreciation of the course of pathological events, and an analysis of the cerebrospinal fluid—the keystone to the situation—materially assist in making an early diagnosis and in instituting a rational line of treatment. Under normal circumstances the mechanism controlling the secretion

of cerebrospinal fluid and its ultimate passage into the venous system is so delicately poised as to ensure an equable pressure. Let this mechanism be disturbed ever so slightly by factors which tend either to cause an increased exudation, or to prevent the passage of fluid through the Pacchionian bodies, and we have at once certain changes induced, changes which are capable of being accurately registered by modern chemical tests.

Under normal circumstances the cerebrospinal fluid is, under slight pressure, 20 to 30 mm. of mercury, has an alkaline reaction, and a specific gravity of from 1005 to 1008. It may be secreted in great amount as the result of some peripheral focus of irritation with, as a consequence, the various signs and symptoms of increased intracranial tension, but so long as it is able to deal with, and to annihilate, any bacterial attack it remains alkaline and more or less clear. Increased turbidity, however, does not mean that it has become septic, but that there has been a marked leucocytosis, in other words, a supreme effort to ward off invasion. Diminishing alkalinity denotes, to my mind, progressive bacterial invasion, while an acid reaction indicates that definite purulency has become established.

My opinion is that all cases of purulent meningitis are preceded by a stage of serous meningitis, when a desperate fight is made by the meninges and cerebrospinal fluid to resist bacterial invasion. To attain victory cerebrospinal fluid has to be secreted in such quantity that the patient may become almost comatose from increased intracranial tension. If, however, operative interference be undertaken at this stage and the focus of infection removed, with at the same time a fair amount of cerebrospinal fluid, recovery not uncommonly follows. That the fight may be a long and desperate one is evidenced by the case of H. R., a female, aged 36, who for five weeks struggled against bacterial invasion of her cerebrospinal fluid and finally succumbed to a streptococcal infection. At the time of her admission to hospital she was suffering from suppurative labyrinthitis and symptoms of increased intracranial tension. Examination of the cerebrospinal fluid, which was turbid, showed a marked leucocytosis, but no bacteria were found either in films or cultures. The fluid was under high tension, contained an increased amount of albumin, and reduced Fehling's solution normally. A complete labyrinthectomy was performed and a small extradural abscess at the apex of the pars petrosa opened. Later, on account of the persistence of increased intracranial tension, translabyrinthine drainage was instituted. The cerebrospinal fluid, which was examined from time

to time, remained turbid and alkaline until two days before the patient's death, when it suddenly became purulent and was found to swarm with streptococci and staphylococci.

Transition from the serous to the purulent type of cerebrospinal fluid is not necessarily, however, indicated by the presence of bacteria. It may and does take place before any bacteria are discovered in films or cultures, as what we have to deal with is the inter-reaction between the toxic by-products of bacterial life and living tissues. It is consequently to the chemistry of living tissues such as the cerebrospinal fluid that we have to look for the earliest indications of pyogenic invasion. Careful analysis will reveal delicate pathological changes at a time considerably anterior to that at which the more gross clinical symptoms manifest themselves. Metabolism of the products of bacterial life is such as to destroy or partially destroy the existing carbohydrates or proteins in the cerebrospinal fluid. It is now admitted that in normal cerebrospinal fluid there is a carbohydrate—a glucose—which has the power of reducing the copper in Fehling's solution. In the presence, however, of bacterial infection of the cerebrospinal fluid the existing carbohydrates become rapidly used up, with the result that in purulent meningitis there is an absence of this copper reduction. Hence we have at once an easy and apparently a certain test (Kopetzky) of determining when and whether a serous meningitis is becoming purulent or not. In addition the percentage of solids is increased, more especially the percentage of albumin. On boiling normal fluid a faint haze from the coagulation of albumin is noted. In purulent meningitis the amount increases at times to as much as 0.1 per cent.

A progressive and at the same time diminishing alkalinity of the cerebrospinal fluid, or a definite acidity, provides another useful bedside test of what is taking place. Several observers, among others Araki and Zillensen, have shown that in the presence of a lack of oxygenation there is a production of lactic acid in the living tissue. Where metabolism is upset as the result of some inflammatory, and more especially septic process, where, in other words, the production is in excess of elimination, a varying amount of acidosis is induced, and it is to this artificial acidosis that the acid reaction of the cerebrospinal fluid is due. So long as the cerebrospinal fluid remains alkaline, even though turbid, there is reason to expect a good result from operative interference, but should it become excessively turbid and acid the prognosis is grave, as then we know that the cell resistance of the individual has been overcome, and that bacteria and their toxins have gained the upper hand.

In the early stages of meningitis the cellular elements found in the cerebrospinal fluid are very much the same as those found in normal fluid. Occasionally a few lymphocytes in various stages of disintegration and a few polymorphonuclears are to be seen. Later on, when the fluid has become definitely purulent, there is an enormous increase in the number of leucocytes, chiefly polymorphonuclears, and a moderate increase in the number of lymphocytes. Bacteria are not found in films or in cultures in the early stages of the disease. As the disease progresses they are, as a rule, easily detected, either intra- or extra-cellular. The commonest varieties found are streptococcus, staphylococcus, a Gram diplococcus, and Friedländer's bacillus.

Coincident with these delicate changes in the cerebrospinal fluid certain clinical signs and symptoms of diagnostic value make their appearance. Thus the gradual increase of intracranial pressure from excessive and protective secretion of cerebrospinal fluid is accompanied by a simultaneous increase of general blood-pressure and progressive tendency to cerebral anæmia. Owing to the brain substance itself being incompressible the pressure is exerted upon its vascular supply, with the result that nutrition is gradually cut off and a condition of malnutrition started. To this progressive increase of intracranial tension too much importance cannot be attached. It is in many cases the determining factor in the fatal issue, the cerebral anæmia which it induces paralysing the function of one or other of the sensitive vital nerve-centres. It is at this stage, the stage of active resistance by the cerebrospinal fluid to the invasion of bacteria, when the fluid, although possibly turbid is still alkaline and capable of reducing the copper in Fehling's solution, that lumbar puncture as a therapeutic measure is so advantageous. The withdrawal of a quantity of fluid, the amount varying with the pressure under which it escapes through the trocar, by relieving the mechanical symptoms due to increased pressure, tends to ward off profound cerebral anæmia and so to give time for the institution of more definite remedial measures.

Another indication of commencing meningitis is found in the presence of an œdema of the optic disk. The sheath of the optic nerves being a continuation forward of the membranes of the brain and containing cerebrospinal fluid, anything which tends to increase the amount of cerebrospinal fluid, and consequently intracranial pressure, will at the same time increase the pressure around the nerve, an increase reflected by a certain fluffiness of the margins of the disk. I have also found in a few cases a lowering of the upper tone limit due to what I take to be similar mechanical causes. Owing to the fact, however, that

the labyrinth upon the affected side is so frequently implicated in the primary septic process the test has in such cases to be applied to the labyrinth of the opposite ear.

The various chemical tests and the signs and symptoms just detailed are evidence of a *prima facie* case of incipient meningitis, and afford sufficient evidence to convict and to banish the invading party. To be effective, punishment should be drastic and rapidly carried out.

In the early stages of meningitis, when the cerebrospinal fluid is under high tension, clear or faintly opalescent, alkaline in reaction, and on boiling capable of reducing the carbohydrates present, repeated or continuous drainage through the lumbar theca, in addition to the removal of the primary focus of infection by so diminishing intracranial tension and consequent cerebral pressure, may bring about a complete cure. Ventricular drainage, although it may find a place in the treatment of non-pyogenic meningitis, entails the risk of infecting a previously non-infected ventricle as well as the cerebral substance through which the knife or needle has to pass. Lumbar puncture is to my mind, however, much more a diagnostic than a therapeutic measure, and although in mild cases it may succeed in bringing about a cure, is not to be relied upon. Even continuous lumbar drainage, which *a priori* might have been expected to be efficient, fails after a time because, as fluid is continuously withdrawn, the brain stem sinks down into the foramen magnum, with the result that it is prevented from flowing from the distended ventricles through the foramen of Majendie and so into the spinal theca. A more effective and more rapid method of drainage is necessary, such as is obtained by translabyrinthine drainage or one or other form of decompressive operation. The internal administration of urotropine is said to have a beneficial effect and to assist in keeping the cerebrospinal fluid aseptic. Its rapid elimination, partly as formaldehyde, and the fact that it is found in the cerebrospinal fluid soon after its administration by the mouth, has given rise to the idea that it might possess a certain antiseptic value, in addition to which Barton and Brown maintain that it is also found in the secretion from the infected ear.

When, in cases of serous meningitis, the labyrinth is the primary focus of infection, its complete removal, with, in addition, the establishment of translabyrinthine drainage as recommended by West and Scott, may prove efficient. In preference, however, to translabyrinthine drainage I am in favour of a decompression operation in the posterior fossa at some distance from the original focus of labyrinthine suppuration



on account of the risks of infection of the cerebrospinal fluid, unless asepsis be maintained, which, under such circumstances, is extremely difficult, if not impossible.

Opinions differ very much as to the actual value of serum therapy and vaccine treatment in cases of purulent meningitis. While not denying that the administration of an autogenous vaccine may help, my experience has been to regard it merely as an adjuvant, and to rely upon the relief of intracranial pressure as afforded by one or other form of decompressive operation, and the removal of the primary focus of infection.

To be successful, any treatment of otitic purulent meningitis presupposes elimination of the primary focus of infection, whether it be a middle or an internal ear suppuration, or, as is so frequent, of the two combined. It is only of late years that purulent internal ear disease has received anything like adequate attention. In my opinion the internal ear is not only by far the most frequent avenue of infection to the meninges, but is also the most dangerous because it leads to direct infection of the posterior fossa. In actual practice, cases of what one might name "tympanic meningitis" are not nearly as fatal as cases of "labyrinthine meningitis." In the former the resulting meningeal infection is likely to be localized, whereas in the latter there is a tendency to rapid diffusion, while from the conformation of the parts operative interference is considerably more difficult. The fact that in the posterior fossa there is a larger amount of cerebrospinal fluid to be infected than in the middle fossa adds to the danger of infection in this region. When, therefore, infection is by way of the internal ear, as can usually be established by the employment of the caloric or other labyrinthine tests, a complete labyrinthectomy in addition to a complete post-aural operation should be performed. Having eliminated the primary focus of infection, any pathological tract leading into the interior of the cranium should be followed, and if a localized collection of pus be found, free drainage afforded by removal of as much of the surrounding bone as is deemed necessary, carried out. Assuming, however, that there is no evidence of any localized collection of pus, but that we have to deal with a spreading meningitis, the difficulties of treatment are enormously increased. The objects to be borne in mind after removal of the primary focus of infection are: (1) The relief of intracranial pressure; (2) the establishment and maintenance of free drainage from the meninges, and (3) the overcoming of the existing toxæmia.

In undoubted cases of purulent meningitis lumbar puncture has no



place other than as a means of diagnosis. Some form of decompressive operation is called for, the essential feature of which is to provide by a sufficiently free removal of bone a window large enough to efficiently relieve existing pressure, and at the same time to provide a means of freely draining the infected meninges. A window having been made either in the temporo-sphenoidal or cerebellar area, the dura will be found to bulge into the opening and to practically cork it up. Some operators content themselves with the making of such a window and with the relief of pressure thus obtained. No doubt in certain cases of incipient meningitis—meningitis serosa—this is sufficient, but in purulent meningitis it merely delays the fatal issue a few hours or days.

To drain the pia-arachnoid cavity the dura may be dealt with in several ways: (1) By excising narrow strips in parallel rows; (2) by raising as large a flap as the bone wound permits of; and (3) by removing entirely the dura corresponding to the bone wound.

To Charles Ballance we owe the suggestion of attacking meningitis by the occipital route. In 1891 he performed the now classical operation of draining the posterior sub-arachnoid space after trephining the occipital bone upon both sides of the middle line close to the foramen magnum. In 1893 Alfred Parkin proposed drainage of the cisterna magna, while in the same year Ord and Waterhouse drained the posterior fossa after removal of a portion of the occipital bone and incision of the underlying membranes. Since that time isolated cases have been recorded by various observers; some successful, many, however, unsuccessful, from the fact that the operation, however skilfully planned and executed, was undertaken at too late a stage—when, in fact, the patient was almost moribund from excessive intracranial pressure and progressive toxæmia.

Whether decompression be performed over the temporo-sphenoidal or cerebellar area, great difficulty is encountered in dealing with the brain substance itself. The moment the dura has been incised the cerebral or cerebellar cortex, as the case may be, is thrust into the wound by the *vis a tergo* and tends not only to cork up the opening made and so prevent the escape of infected cerebrospinal fluid, but also to lacerate its substance against the edges of the bone wound. Efficient drainage of the sub-arachnoid space is consequently rendered very difficult. The tendency to brain hernia is also encouraged partly from the *vis a tergo* and partly from the mechanical difficulties of maintaining free drainage. To obviate this tendency to brain herniation, Haynes, of New York, has suggested drainage of the

cisterna magna through the cerebello-medullary angle, as in this situation there is no brain tissue in the immediate neighbourhood to protrude, and also because infected fluid is prone to collect here. He regards this situation as the *one logical place* where removal of infected cerebrospinal fluid should be practised. The patient is laid prone upon the operating table, the head being held up by a suitable head-rest or by a competent assistant. An incision is made in the middle line from the occipital protuberance to the spinous process of the axis, the soft parts retracted, and the underlying occipital bone removed. A  $\frac{3}{8}$ -in. trephine is applied in the middle line about 1 in. above the margin of the foramen magnum and a disk of bone removed. The dura is then separated from the bone and two grooves made through the bone into the foramen magnum. When this triangular piece of bone has been removed, the dura presents under pressure. A small incision is made through the bulging dura and arachnoid, with the immediate escape of cerebrospinal fluid. When a quantity of fluid has drained away, the incision is enlarged and an inspection made of the posterior poles of the cerebellum, the notch between them, and the posterior surface of the medulla. A drain is then inserted into the cisterna magna and suitable dressings applied. So far I have only performed Haynes's operation twice, and in neither case did the patient survive. Both cases were advanced cases of purulent streptococcal meningitis, with high arterial tension and pus-laden cerebrospinal fluid; in both cases, I believe, the operation was undertaken too late. The procedure, however, appeals to me, and at some future date I hope to have success with a case undertaken at a much earlier stage of the disease. The position of the patient upon the operating table rather interferes with the administration of a general anæsthetic—possibly spinal anæsthesia might prove sufficient, but of this I have had, so far, no experience.

My records show thirty-seven cases of meningitis serosa so called, with twenty-nine recoveries and eight fatal cases. In these eight cases the cerebrospinal fluid became definitely purulent, and although one or other form of decompression operation was performed it was unsuccessful. Of cases diagnosed at the time of admission to hospital or to surgical home to be suffering from purulent meningitis and submitted to operation I have had fourteen. In four of these cases it probably would have been wiser to have attempted no operation, at any rate all died. Of the remaining ten, where there was at least a sporting chance of recovery, six died and four, or 40 per cent., recovered. This

certainly is nothing to boast of, but is, at least, a step in the right direction.

In conclusion, I would urge the necessity of an early diagnosis, employing for the purpose such tests as I have detailed, followed by immediate operative interference, should such tests prove positive. Although the results of surgical intervention so far obtained are far from satisfactory, I believe the day is coming when, with modern methods of diagnosis and technique at our disposal, the high mortality of the past will shade into insignificance in comparison with the brilliant records of the future. It is for a society such as this to lead in the van of progress, not to be deterred by failure, but to press on to obtain that great reward, the knowledge that our efforts have been crowned with success, and that an otherwise doomed life has been saved as the result of scientific investigation and surgical skill.

#### DISCUSSION.

The PRESIDENT (Dr. J. Dundas Grant) said members would admit that the Section had just heard one of the most refreshing papers to which it had ever listened. Meningitis was particularly interesting to the otologist, because admittedly otitic meningitis was the most dangerous form encountered when compared, for instance, with that arising from nasal conditions, and probably because it affected the posterior fossa of the skull. It was very gratifying to notice the hopeful tone which Dr. Milligan had adopted towards the disease, in which he agreed with what had been expressed by Kopetsky and others in recent discussions. At the commencement of the year a long discussion on the subject took place at the German Otological Society, and there it was said that the best results followed incision of the dura mater. Alexander recently brought forward cases in which that was the determining factor. But he did not think the points concerning early diagnosis were so freely discussed there as in America, and the Section was indebted to Dr. Milligan for having brought them forward. He hoped that, in his reply, Dr. Milligan would formulate what indications as given by the biochemical tests would not only justify but call for immediate operation of a complete kind. The Germans recognized the possibility of spontaneous recovery from meningitis. Though that did occasionally take place, it was not to be counted upon. He would be glad to know whether Dr. Milligan's study of the new methods had led him to know when

the danger-point was within threatening distance. In various diseases undoubtedly the best results were obtained from early recognition and operation; and even where there seemed to be a distant chance of spontaneous recovery, it was better that a few more operations should be performed, if done skilfully, than that an additional life should be lost owing to their omission.

(Dr. Grant then brought before the Section drawings showing the stages in Haynes's operation for sub-occipital drainage of the cisterna magna.)

Mr. C. E. WEST said he was sure he voiced the feeling of the meeting in thanking Dr. Milligan for a most instructive and helpful paper, one which put forward some points new to him, and emphasized others on which there was general agreement. He wished to mention a few points in criticism, not so much of the paper as of the subject. He would like to see the disappearance of the term "meningitis serosa," which he regarded as delusive. There was only one infective meningitis, and the phase of it depended on the period of invasion, on the infectivity of the micro-organisms, and upon the resistance of the patient. Meningitis serosa, plastic meningitis, exudative meningitis, &c., were terms of post-mortem room description, and had little to do with diagnosis or treatment. He acknowledged that in the matter of prognosis one must distinguish between early and late meningitis, but in every case of meningitis the cerebrospinal fluid had certain common characters, and one could not draw lines of distinction. Even with regard to acidity, anyone who had titrated chemical solutions knew that the reaction depended on the sensitiveness of the indicator—i.e., as to whether one called it acid or alkaline. The lumbar puncture needle remained the great means of diagnosis, and he regarded all neurological reactions as of relatively academic interest only. The more refined were one's examinations of the cerebrospinal fluid, the more would one learn about the condition of the patient. The author's phrase "acidosis" was interesting with regard to the cerebrospinal fluid. The causal organisms of meningitis, particularly the streptococci, grown on any medium which contained glucose, all produced an acid reaction, and he felt that the organisms were growing in a culture medium inside the patient's head, and the acid reactions were produced as in broth. Another phrase which he would like to see deleted was "pachymeningitis externa." Why should that be called meningitis at all? If one used the term "extradural abscess" the meaning would be

clear. When there was an abscess outside the peritoneum one did not speak of peritonitis. There was, of course, "ulceration of the dura mater," but the term was dangerous in the sense that it was consecrated to the idea of transdural infection, which was one of the rarest ways in which meningitis occurred. In many cases of meningitis the route was easily provable. In relation to this he would relate a case, the operation upon which delayed his arrival that afternoon. It was that of a girl, aged 13, who obviously had meningitis and a chronic discharge from both her ears. He eventually selected one ear as being the more likely. She had a horribly foul condition in her mastoid, and there was an abscess in the posterior cranial fossa and "ulceration" of the dura mater; it was granulating, but the sinus was not thrombosed. He found no pus inside the labyrinth nor any evidence of infection, except that he raked out some reddish thickened shreds, which might have been the oedematous contents of the vestibule. When the internal auditory meatus was opened pus issued from it. When that had ceased flowing he passed the probe along the internal meatus and an adhesion gave way somewhere; he definitely felt he had passed through a resistance, and then there was a fountain of turbid fluid containing flakes of lymph.

That brought him to the point which he had most at heart—namely, the route for treatment. He confessed that his cases did not show anything like the brilliant results which Dr. Milligan's did; he did not think that at St. Bartholomew's Hospital they saw the cases so early. Most of the cases were, like that he operated upon that afternoon, purulent meningitis, as Dr. Milligan would group them. But even in cases of so-called purulent meningitis recovery without drainage or a decompression operation was possible. He had seen pneumococcal meningitis get well after an ordinary mastoid operation. Other cases, even when purulent, would get well from repeated lumbar puncture, with the injection intravenously of salines and other measures. That was not to be interpreted into his being in favour of treating these cases without drainage, but it was necessary to preserve one's perspective as to the values of the measures employed. He had tried the decompression operation with incision of the dura mater at various times, and his experience was that one had a very encouraging flow of fluid at the moment, but whatever one did, the brain came into the opening in the dura mater, and in twenty-four hours, even with gauze drains, the brain was soldered down to the margin of the drain, and but little drainage was subsequently procured from that opening. And there would probably

be left a hernia of the brain which might give trouble a couple of years, if the patient lived long enough. The operation depicted on the screen seemed less likely to be followed by herniation of the brain. He had a particular affection for Nature's own drainage-tube—i.e., the internal auditory meatus. In using that, one was following the route of infection, the tube was in the right position, and in the case of obstruction a probe could be passed down as often as necessary without risk of injuring brain tissue, while the risk to the facial nerve was not a great one. Drainage by that means could be kept up for seven or eight days, and at little expense of the patient's vitality through the extension of the operation, for it must be remembered that these patients were exceedingly ill. That was the great objection to the anatomically good operation which had been depicted on the screen, for every ten minutes spent on the operation narrowed the chances of recovery. If it was simply a question of draining the infected labyrinth, to prevent or minimize the further invasion of the meninges from the labyrinth, simple opening of the labyrinth below the facial nerve by what was called inferior vestibulotomy was, in his opinion, adequate. He regarded complete labyrinthectomy as unnecessarily severe.

Lest it should be thought that his remarks were meant as an attack—he was sure Dr. Milligan did not think so—he desired to end as he had begun on the note of thanks to Dr. Milligan and congratulation of the meeting.

Mr. SYDNEY SCOTT joined in the expressions of appreciation of Dr. Milligan's paper. Mr. West had alluded to nomenclature, and he would like to add the word "subdural" to Mr. West's list. He hoped Dr. Milligan would agree to a preference for such term as "intradural" or "extradural," whichever might apply. He had been thinking that the path of evolution of treatment of meningitis seemed to have followed that of infective peritonitis. This was, of course, chiefly a question of early diagnosis. Often in earlier times when the diagnosis of infective peritonitis was made, the patient was *in extremis* when operated upon. A free incision was made, the intestines were drawn out on to the table, washed and sponged, and the peritoneal cavity flushed out in a very painstaking and thorough manner, but with the inevitable result, that if he survived the procedure at the time it was only to succumb soon afterwards. As the early diagnosis of infective peritonitis became more accurate, so the operations necessary for its relief became less severe. He believed it would prove to be the same with the meninges, which



could cope with certain degrees of infection, just as the peritoneum can. Of his own cases of leptomeningitis, those in which he had performed extensive decompression operations with drainage of the ponto-cerebellar recess and basal cisternæ, had all been fatal; whereas the successful cases were those in which (a) translabyrinthine drainage had been performed (in cases of meningitis secondary to labyrinthine infection); (b) while in cases of meningitis not due to labyrinthine infection, simple lumbar puncture combined with the mastoid operation had succeeded. He had related such cases at the Manchester meeting last year, and there referred to the influence of early diagnosis and immunity. He felt sure that the simpler measures which Dr. Milligan had described would be the rule in the future.

Dr. DAN MCKENZIE expressed the pleasure with which he had listened to Dr. Milligan's paper, which presented many illuminating suggestions and raised many interesting problems. The necessity of early diagnosis and treatment, if the latter was to be successful, would be obvious to all. He would emphasize the diagnostic importance of pain—occipital headache associated with some rigidity of the neck. Eliciting the latter was very simple: as the patient lay on his back, one placed the hand under the head and bent it a little forward, keeping the spare fingers of the same hand on the nape of the neck. In early meningitis one could thus elicit early rigidity of neck muscles. Occipital headache, whether combined with this rigidity or not, should lead to lumbar puncture and examination of the fluid. The oftener lumbar puncture was performed in such a case the better for the patient. There were cases in which examination of the fluid was negative and yet meningitis was present. In those cases, particularly, the early signs of rigidity were important. It was agreed that treatment resolved itself into removal of the focus and drainage of the sub-arachnoid space, or at least of the sub-arachnoid spaces in the immediate neighbourhood of the disease focus. But the problem which attracted them, and would undoubtedly demand attention in the future, was that of general purulent meningitis and its treatment—namely, that condition in which the disease had passed the incipient stage and was entering the realm of the desperate. Dr. Milligan had described the decompressive and other large operations for desperate cases. With regard to the occipital operation he had described, there had been six cases so far in which it had been done, and without a success; the original author's own cases were all fatal, though in one there was a lightening of the



symptoms immediately after the operation. So one could not, at present, expect much from it. Some theoretical difficulties arose in considering the question of these and other large decompressive operations. Most speakers laid much stress on the mechanical effects on the brain of the pathological process, but one must also consider the toxic effects of the bacterial products on the nerve cells, and that while it was right to try to obviate the mechanical disabilities, one had also to deal with the vital difficulties just mentioned. Stoddart Barr, of Glasgow, proposed and carried out—though in the particular case not successfully—a washing through of the cerebrospinal fluid from the brain to the spine by means of some chemical solution. Another possibility was that, instead of having one large decompressive operation, or one large area drained, one should institute a series of multiple drainage points, which would at once secure more efficient drainage and reduce the liability to hernia. With regard to the parallelism between meningitis and peritonitis, in the worst cases of peritonitis multiple drainage had been carried out, and similarly he would favour multiple trephining and multiple drainage in the region of the base of the cranium in severe general purulent meningitis.

The PRESIDENT asked Dr. Milligan to be good enough, in his reply, to formulate the signs calling for operation; no doubt he would agree that the tests of the cerebrospinal fluid should be taken along with the clinical symptoms, that one sign should not be taken alone. He would be interested in knowing, also, whether Dr. Milligan found, with the Germans, that cases of staphylococcal meningitis were exceptionally favourable. No speaker had referred to Kernig's sign, and it might be interesting to note that a prominent neurologist had recently stated that their difficulties would have been less if that "sign" had never been discovered. This discussion on meningitis had been one of the most concise and objective debates that the Section had held, and it dealt with one of the most difficult and diffuse subjects which could be chosen. He was sure the Section would tender its formal thanks to Dr. Milligan for having opened the discussion.

Dr. MILLIGAN, in reply, thanked all who had spoken for their appreciation of his efforts to make the discussion interesting. In answer to the President, what he specially wished to formulate was that serous meningitis was only part and parcel of a general advancing disease; and he agreed with Mr. West that it would be much better

not to use the term. But it was a great responsibility for one to try to delete a term altogether, even if one did not believe in its exactitude. It would be better to regard the disease as simply a general infective process, at a certain stage of which there was a watery exudation, which ultimately became purulent. The so-called serous condition he believed to be purely the result of an effort of Nature to protect the individual. The more acute the invasion, the more fluid was thrown out for protection. The great point was early diagnosis. Mr. Scott had referred to the severity of some of the operations, but they were carried out only in the most desperate type of case. The object should be to deal with the cases before they became so desperate. When they were desperate a mere lumbar puncture was useless. He believed there were certain chemical changes which were distinctly in advance of the clinical signs and symptoms, and that examination of the cerebrospinal fluid was the keystone to the situation. If the carbohydrates had been used up—i.e., if there was failure to reduce the copper in Fehling's solution—it showed that pathological changes due to pyogenic infection were going on in the fluid. Diminishing alkalinity—not necessarily an acidity—was the sign that something pathological was in progress. If something radical was not done, meningitis purulenta would supervene straight away. One did not neglect the clinical signs and symptoms, but it took some time for them to appear. Rigidity of the back of the neck did not occur very early, and though it was easily detected in posterior fossa meningitis, it was not so in middle fossa meningitis. In answer to Mr. West, he did not call his (the speaker's) own results brilliant, but his present results were better than previous ones. Not many years ago there were 100 per cent. of deaths, and he believed the present mortality-rate would be considerably reduced if all the points mentioned were taken into account, and the proper type of operation instituted. His own objection to translabyrinthine drainage was the fear of infecting the meninges, and where the translabyrinthine operation would do good so also would a small decompression operation. Mr. Scott's comparison of meningitis with peritonitis was a happy one, and it was true that operations for peritonitis were becoming less severe. But why? Only because the disease was now recognized and operated upon much earlier, and the same thing would happen in purulent meningitis. He agreed that spontaneous recovery occurred in certain cases, but that depended on the degree of virulence of the organism. It was not, however, his experience at hospital, where cases were generally brought in late. He had not seen a case of staphylococcal

or streptococcal meningitis recover without some operation being done. Pneumococcal meningitis seemed to recover spontaneously sometimes. With regard to the operation of tapping the lumbar theca and washing through, referred to by Dr. Dan McKenzie, that was a very old suggestion and had now been given up, as had also the injection of various fluids, among them a preparation of silver. The thing to aim at was more delicate chemical testing of the cerebrospinal fluid, and earlier operation.

Dr. DAN MCKENZIE asked, further, whether, in a case of suppurative disease in the ear, in which other signs of meningitis were absent, but in which the cerebrospinal fluid was found by chemical test to be deficient in carbohydrate and acid in reaction, Dr. Milligan would advise immediate drainage of the sub-arachnoid spaces.

Dr. MILLIGAN replied that if he had a case of chronic suppurative middle or internal ear disease, with the temperature going up and arterial tension increasing, with diminishing alkalinity of the cerebrospinal fluid and absence of copper reduction on boiling with Fehling's solution, he would recommend a decompression operation, because such a case was obviously tending towards purulency, and one was justified in operating at once to prevent it.

## Otological Section.

February 21, 1913.

Dr. J. DUNDAS GRANT, President of the Section, in the Chair.

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### An Examination of both Temporal Bones from 120 Individuals, made with the view of deciding the Question of Symmetry.<sup>1</sup>

By ARTHUR H. CHEATLE, F.R.C.S.

MR. CHEATLE said it was unnecessary on this occasion to go through the description of the specimens, as he had already shown them last October, and the details could be read in the *Transactions* of the last International Congress of Otology which was held in Boston. The specimens are now in the Royal College of Surgeons Museum. He showed lantern slides of some of the more interesting points. Symmetry was present in eighty-two, and asymmetry more or less marked in thirty-eight. The diploetic infantile type which is so important in suppuration was present in forty-four, in twenty-four on both sides, and in twenty on one side only; of these twenty-seven were so asymmetrical as to affect the course of suppuration and X-ray photography, that is to say, that the diploetic type which would give a dark shadow was present on one side and a cellular mastoid on the other. Marked symmetry of the mastoid cells was shown in several sets. The extension of cells into the digastric fossa sometimes caused a "digastric bulla" on one side only, or unilateral extension into the occipital bone caused an "occipital bulla." The lateral sinus and sulcus jugularis were larger on the left side in thirty-two sets.

The PRESIDENT (Dr. Dundas Grant) said he was sure members would agree that the Section had cause to feel proud of Mr. Cheatle's work, and he

<sup>1</sup> Referred from the meeting on October 18, 1912.

would remind them that Mr. Cheatle had been awarded the Lenval Prize for the work he had done as of the greatest value to otology. Most would agree that Mr. Cheatle had shown that though the chances were in favour of symmetry, on the whole the exceptions were also very numerous.

### **Osteoma of the Mastoid.**

By E. B. WAGGETT, M.B., and E. D. DAVIS, F.R.C.S.

A CASE very similar to that exhibited at the November meeting. A woman, aged 36, complaining of deafness of four months' duration, and who had discovered the presence of the tumour accidentally. A hard hemispherical tumour the size of a bantam's egg projected behind the ear in the antral region, and also obstructed the meatus. Deafness of obstructive type.

Operation: Skin incision following contour of growth. Hugh Jones's meatal flap attached by a pedicle consisting of the whole of the tissue, less the skin, elevated off the tumour. The contour of the tumour proved to be sharply defined from the normal outer table by a groove. As the position of the lateral sinus could not be made out in the skiagram, a trench was carefully cut with the electric burr until mastoid cells and normal diploe were exposed at all points, when a few taps of the chisel brought the tumour away. Its inner aspect proved to be well defined, and the tumour, which measured 1 in. by 1 in. by  $\frac{5}{8}$  in., was of a flattened ovoid shape, and consisted throughout of dense bone. After the removal of wax, the drum-head was seen to be normal, and the mastoid process to be of the pneumatic type with a large antrum separated by a shell of bone from the sinus; all mastoid cells were removed, and in lining the large cavity created Hugh Jones's flap was found very convenient to manipulate owing to its long and flexible pedicle; it is suggested that the flap might with advantage be split longitudinally in order to furnish eight growing epithelial edges.

Photographs were shown for the purpose of emphasizing the advantage of stereoscopic over ordinary photography for demonstration purposes.

### **DISCUSSION.**

Mr. CHEATLE said it had been suggested that in order to make the X-ray picture of the temporal bone easier to interpret, the external auditory meatus should be filled with bismuth paste.

Mr. JENKINS asked whether the osteoma was entirely within the mastoid, and not reaching the surface, either through the meatus or externally.

Dr. URBAN PRITCHARD said he had encountered two instances of the condition. One was a specimen which Mr. Harvey had; it was simply sawn off, and the bone proved to be very dense. The other patient had the condition symmetrically, and it had persisted twenty-five years without causing her trouble.

Mr. WAGGETT replied that it was an osteoma of the outer table, and projected like a chestnut at the back of the ear, and into the meatus, obstructing it. In this operation he found Mr. Hugh Jones's flap very valuable, owing to the large cavity left by the removal. He asked if any member had split the skin element of the flap into two or three portions, so as to obtain a wider-growing edge.

### A Periosteal Lining Flap in the Radical Mastoid Operation.

By P. WATSON-WILLIAMS, M.D.

FIRST incision extends from just above the highest point of attachment of the pinna, curving outwards and backwards, well within the margin of hairy scalp, curving forwards below to the mastoid tip. The

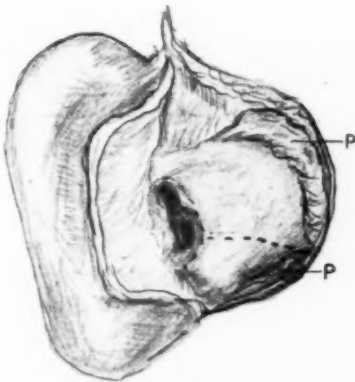


FIG. 1.

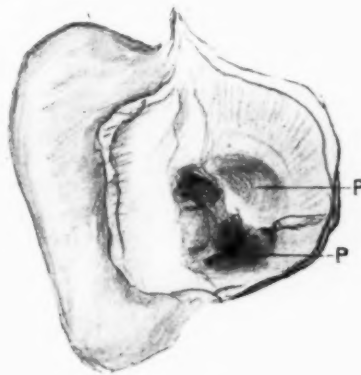


FIG. 2.

Fig. 1.—The skin and soft tissues over the mastoid eminence have been reflected forwards; the periosteum, after making incisions indicated by the dotted lines, reflected back (P, P).

Fig. 2.—The mastoid operation has been completed as far as removal of bone, &c., and the periosteal flaps brought forwards and utilized to line the bone cavity as far as possible.

skin and soft tissues, save only the periosteum, are dissected forwards to the margin of the bony meatus.

Second incision divides the periosteum along the superior and posterior margins of the bony meatus, a third incision being carried horizontally backwards from near the lowest point of the meatal incision, so that the whole of the mastoid periosteum, excepting that of the tip, may be reflected backwards and upwards.

After conclusion of the operation, after the meatal flap has been made, the periosteal flap is brought down over the upper and posterior wall of the resulting mastoid cavity, and retained *in situ* by the packing. With Körner's flap the packing lies between the periosteum and the flap. The mastoid periosteum is usually saved only to be replaced between the deep surface of the skin and the external or raw surface of the concho-meatal skin-flap, serving less useful purpose. The method described starts the posterior and inner walls of the mastoid bone cavity with a periosteal covering which quickly attaches itself to the bone and thus promotes rapid granulation over which the epithelium from the edges of the concho-meatal skin-flap extend rapidly. The more rapid formation of granulations lessens the size of the healing cavity, and thus decreases the area for epithelialization.

#### DISCUSSION.

The PRESIDENT said he presumed the flap speedily became covered with granulations. The Section was honoured by a visit from Dr. Coghlan, of Portland, Oregon, and perhaps he could say what had been done in America in this respect. He would like to know whether Dr. Watson-Williams found that his method shortened the duration of after-treatment: or whether it diminished the size of the after-cavity without leaving the little recesses which gave so much trouble. It would be agreed that the desideratum was to come as near the results obtained with skin-grafts as possible. Mr. Hugh Jones's method seemed to keep up the nutrition of the skin-flap which was turned in, and it presented the greatest amount of ingenuity and aptitude for the purpose. The only objection to the skin-graft was that it generally meant a second anæsthetic and operation.

Dr. URBAN PRITCHARD asked whether Dr. Watson-Williams considered that a covering of epithelium formed more quickly than if it were bare bone and ordinary granulations were left to form. He had always wanted to have a method of filling up the new cavity as much as possible; it would save much subsequent trouble.



Mr. CHEATLE said he believed the method had been anticipated by an American surgeon, as he remembered reading a description of a periosteal flap. It was very important to recognize priority; and he felt sure this was not new.

Dr. COGHLAN (Portland, U.S.A.) expressed his pleasure at being permitted to attend the meeting of the Section, which he found very instructive. He had never previously seen the flap now described by Dr. Watson-Williams, and did not know that it had been described in the States.

Mr. C. E. WEST considered the question of speed of healing was important. He could see that periosteum laid down in that way would take, because it was periosteal graft on bone. But his own experience of periosteum was that it was about the most obstinately granulating tissue in the body, and that it was difficult to get epithelium to spread over the granulating periosteum. Why not put a skin-graft on bone? It would adhere. Though Dr. Watson-Williams's method was ingenious, he was somewhat doubtful of the practical gain by a procedure which included the grafting of periosteum in the walls of the mastoid cavity.

Mr. SYDNEY SCOTT said that during the last three years he had made use of a periosteal flap which he reflected downwards and backwards, instead of upwards as described by Dr. Watson-Williams. He had not regarded the procedure as one of any particular importance; it simply amounted to this, that instead of cutting away the periosteum, as he had once been accustomed to do, the periosteum covering the outer surface of the mastoid process was retained, and when packed into the operation cavity it helped to fill it up, so that less packing was required, and the skin-graft which was applied at the same time need not be quite so large.

Mr. CHARLES HEATH said the pericranial flap which he had devised, and used for many years in acute and chronic, radical or conservative operations, was a rather smaller one than that now depicted by Dr. Watson-Williams, the upper incision defining the flap being, like the lower one, horizontal. He had recently sent Dr. Watson-Williams a reprint from the *New York Medical Journal*, of August 10 last, of an article by Dr. Leslie, of Toledo, Ohio, in which he (Dr. Leslie) described the flap. He (the speaker) had used such flaps in all cases since 1906—i.e., in many hundreds of operations—and if he had found any reason to vary it he would have done so long ago. He was sure, therefore, Dr. Watson-Williams would find it a very useful flap.

Dr. DAN MCKENZIE said he had used Mr. Heath's flap for a long time, and at the operation it looked very nice, but his own feeling was much in the same direction as Mr. West's, that it was very prolific of granulations; there seemed to be a tardiness of epithelialization after a periosteal flap, which was not seen in the Hugh Jones flap. The latter he had used three times recently, and in these cases epithelialization was complete in about six weeks.

Mr. HUGH JONES said he saw Professor W. L. Ballenger operate last summer, and he laid stress on the retention of the periosteum, but he did not think that surgeon made any formal flap. After cutting round the meatal margin, and making a horizontal cut backwards, he just turned the periosteum in. He wondered what was the effect of that and similar procedures on the growth of bone. When cases operated upon years ago, in which, presumably, the periosteum was destroyed or removed, were opened up again, there was found to be lipping of the bone, and sometimes the cortex seemed to have grown over so as to almost obliterate the surface opening but leaving a large cavity within. Sir William Macewen's well-known researches on the relation of periosteum to the growth of or limitation of growth in bone were interesting in this connexion.

Mr. MARRIAGE, remarking on the President's statement that the objection to grafting was that it required a second anæsthetization and operation, said that for years he had put the graft on at the time of the first operation ; then there was no occasion to worry about the flaps, and the graft would take in every instance. Epithelialization of the cavity occurred in three or four weeks, and that seemed the ideal method. He always used the graft which was first introduced by Mr. Ballance.

Dr. COGHLAN said he agreed with Mr. Marriage about the flaps, and in his part of the States all did primary skin-grafting, and with very good results. Some of his confrères in San Francisco had had some wonderful successes in such cases. Primary skin-grafting certainly seemed to be the best.

Dr. WATSON-WILLIAMS replied that some time elapsed before granulations sprang up on the bare bone of the mastoid cavity, but the periosteum attached itself quickly to bone, its natural habitat, and the cavity then granulated up more quickly. In answer to the President, Dr. Watson-Williams could not give, off-hand, the number of cases in which he had used it, but only his general impressions, and after all statistics were really of less value than an impression resulting from many experiences, because of the variability of the sizes of cavities dealt with ; and his impression was that the method certainly shortened the period of healing. The grafting of the periosteum made the cavity smaller, hence there was less space to fill up. Hence, even if the rate of epithelialization were less, it would be compensated for by the smallness of the cavity to be covered. He had used the method for some years. He did not refer to the reprint sent him by Mr. Heath, because he thought it would be better for the latter to speak for himself, but the method described by Leslie was a very different procedure, a triangular flap of periosteum being retracted, and replaced beneath the concho-meatal cartilage used to line the floor.

### **Otitic Abscess of the Pterygoid Region drained through the External Auditory Meatus ; Recovery.**

By DAN MCKENZIE, M.D.

THE pterygoid abscesses followed suppurative labyrinthitis with facial paralysis in a case of chronic suppuration of the middle ear.

Male, aged 20, was admitted to the Central London Throat and Ear Hospital, on August 21, 1912, with suppuration of the left ear and facial paralysis.

History : Purulent discharge and deafness in the left ear of eighteen years' duration, attributed to scarlet fever. Some increase in the discharge during the last two weeks. Sudden appearance of facial paralysis five days before admission. Never any vertigo, nausea, or vomiting.

Present condition : There is a large perforation in the postero-inferior segment of the membrana tympani. No pain, tenderness, or swelling of the mastoid region. Hearing : Does not hear watch on contact. Weber lateralized to the right ; Schwabach + 5 ; Rinné minus. No loss of high notes with Galton's whistle, but with Bárány's noise-machine in the right ear the patient was unable to hear any sound in the left. Slight, spontaneous nystagmus to both sides, but rather more marked to the right.

August 22 : Radical mastoid operation and labyrinthotomy. The mastoid antrum was small and deeply situated. Disease of the bone was found to be chiefly located in the region of the aqueductus Fallopii. A fistula was discovered in connexion with the external semicircular canal. The fistulous opening was enlarged, the outer wall of the canal being broken down with the labyrinth chisel. Inferior vestibulotomy was then performed through the wall of the promontory.

After the operation the patient did not make good progress. There were occasional evening rises of temperature to between 99° and 100° F., and pain was complained of in the ear and left side of the head, apparently radiating from a spot about half an inch below and in front of the mastoid process. Purulent discharge continued to flow from the ear, the auricle became inflamed, and the post-aural wound did not unite ; in short, the operation area looked as if it had become septic. As time went on, the local inflammation subsided, although the headache continued.

On September 21, lumbar puncture was performed, and 20 c.c. of clear cerebrospinal fluid was withdrawn. Next day the headache had disappeared, and as the other symptoms were moderating the patient was discharged, although he still continued to attend as an out-patient.

For a month the ear continued to discharge more or less. And on October 23 he complained of severe pain in the ear and head, with swelling of the face. There was marked œdema of the left side of the face, affecting chiefly the temple and zygomatic region, and also the left cheek and orbit. He complained also of pain on eating, so severe that he was unable to masticate his food. On examination it was seen that the lower jaw was fixed in a half-open position. Attempts to open the mouth wider or to close it gave rise to much suffering. Pain was also felt on swallowing, and on inspecting the throat marked swelling and redness of the left tonsil and left side of the pharynx were observed. Temperature: 100·6° F. No rigors.

A diagnosis of pterygoid abscess was made, and on October 24, under chloroform, the post-aural wound was re-opened, the auricle being reflected well forward. The anterior wall of the osseous meatus was then exposed, and removed with a gouge in such a way as to form a window through it, deep to the temporo-mandibular articulation, and close to the tympanum. On removing the bone a considerable quantity of pus under pressure flowed into the meatus. After the evacuation of the abscess a probe was inserted into the cavity and passed down towards the pharyngeal region, where its point could be felt with the finger in the mouth. The bone of the under surface of the petrous portion seemed to be bare. The cavity was packed with gauze and the auricle was replaced; but the post-aural wound was left open for drainage and inspection.

Intermittent fever continued for a week after the operation, and then the temperature fell to normal. The œdema of the face rapidly disappeared and with it the stiffness of the jaw. Relief to the pain was experienced immediately after the operation. A few weeks later the cavities had closed and the ear had become epithelialized. The facial paralysis remains.

Otitic pterygoid abscess, or pharyngeal abscess as it is sometimes called, seems to be a very rare complication of purulent otitis, as only some fifteen cases have been recorded. Most of these have been drained by pharyngeal incisions. As far as I have discovered the route successfully adopted in this case does not seem to have hitherto been tried. Attention is directed to the group of symptoms manifested by this

patient, which was so characteristic as to lead to the correct diagnosis of the seat of the abscess.

I am indebted to Mr. Ryland, House Surgeon to the Hospital, for his careful notes of this case.

#### DISCUSSION.

Mr. A. CHEATLE said he had been concerned with three instances of this trouble. The first was a specimen which he found post mortem, in which there was an abscess lying behind the jaw, and a carious opening in the meatal wall, leading to the abscess. The patient was operated upon by his brother fifteen years ago, and death resulted from leptomeningitis and temporo-sphenoidal abscess. There was a definite hole in the meatal wall leading to the abscess cavity, and a rod was passed through it. The second case he operated upon, and it had much the same characteristics as Dr. McKenzie's; it was reported in the *Transactions* of the old Otolological Society, vol. viii, p. 45. At the operation he found a labyrinthine sequestrum. The anterior meatal wall was replaced by a granulating hole and his finger could pass through that into a big abscess cavity behind the jaw to the tonsil. He did not drain the abscess through the pharynx, but put an aneurysm needle into the depth of the cavity, brought the point up into the neck, and made a counter-opening in a line with the anterior border of the mastoid process. The case did very well. The third case he saw in consultation, and there the trouble in the anterior meatal wall led to an abscess, which pointed into the pharynx, where it burst. Dr. McKenzie did not suggest how the pus got to where it did. He (Mr. Cheadle) suggested it got there by caries of the anterior meatal wall.

Mr. SYDNEY SCOTT recalled having seen one example of suppuration in the region occupied by the pterygoid muscles on the right side, in a patient who died with Bezold's mastoiditis and a temporo-sphenoidal abscess on the same side.

Mr. JENKINS asked whether Dr. McKenzie would adhere to the name pterygoid abscess, as that did not seem to be the situation of the suppuration in this case. He believed the abscess must have been situated external and in front of the tympanic plate and through the deep cervical fascia that passed up deep to the parotid gland to be attached to the vaginal process of the tympanic plate and spine of the sphenoid. This space defined by fascia reached to the lateral wall of the pharynx, and so it was explained how Dr. McKenzie found the abscess reaching that region. The abscess would be deep to the parotid gland.

The PRESIDENT asked what were the indications for opening the labyrinth in this case, seeing that there was an absence of vertigo, nausea, or vomiting. No doubt the labyrinth was destroyed, for all functional purposes. He congratulated the exhibitor on his ingenious drainage.

Dr. DAN MCKENZIE replied that he considered he was justified in opening the labyrinth at the time, but since then he had not felt so clear about it. There had been deep-seated pain, facial paralysis, and total inability to hear with that ear as tested with the noise machine. It was because of the subsequent history of pterygoid abscess that he showed the case. With regard to that name, the abscess was a swelling which was interfering with the pterygoid muscles situated in what the anatomy books called the pterygoid region. No doubt the deep parotid region was involved, but to have called it "parotid abscess" would have given an impression which he did not wish to convey. It began in the ear and so could not be called "pharyngeal abscess." He proposed, therefore, to adhere to the name he had chosen. He was sure there was no caries or bone disease in the bony meatal wall; but with a probe he found the bone bare in the inferior petrous region. He did not think, therefore, the disease had reached the pterygoid region by implication of the bony wall of the meatus.

#### **Specimen from a Case of Epithelioma of the Left Auricle.**

By G. N. BIGGS, M.B.

PATIENT, female, aged 62. The growth had been present for five months, commencing as a small nodule, which in about six weeks began to break down and ulcerate. Previously to appearance of the growth, the auricle had been quite normal, and there was no history of any injury at any time. Slight shooting pain was present at first (four weeks), but there had been none since, neither had there been any attacks of hæmorrhage. One sister died of malignant disease of the uterus. There was no involvement of the lymphatic glands.

#### **Progressive Bilateral Deafness following Epidemic Cerebrospinal Meningitis.**

By H. J. DAVIS, M.B.

THE patient, a boy, aged 6, was sent by Dr. Dixon for an opinion as to whether anything could be done to improve the hearing or not. Three years ago the child had cerebrospinal meningitis and nearly died; the hearing power has since become worse and worse, until, at the present time, he hears nothing with the left ear and with the right ear appears just conscious of sound when a Bárány alarm apparatus is suddenly released in the meatus. He responds to this by closing the eyes, but



as far as could be made out he hears nothing else. Neither labyrinth responds to the caloric tests, and the boy is impenetrably deaf. Hearing no conversation the child naturally speaks less and less, and if not suitably instructed he will become a deaf-mute.

In this country, little assistance seems obtainable for these cases; children are either "too young" or "too old" for the Institutions. They cannot be taught properly at home, and so they drift on, forgetting words already learnt, never increasing their vocabulary, and in course of time making their wants known by signs alone.

Some of my colleagues who attended the Otological Congress at Boston, U.S.A., in 1912, must have been impressed by the efficient way in which these cases are dealt with in America; children are taken in hand at once, properly taught, and so converted into useful citizens. In England the instruction to be obtained with this object in view is totally inadequate to the demand, and the exhibitor is of opinion that it is high time this defect was remedied.

#### DISCUSSION.

Mr. CHEATLE asked why it was called progressive deafness; surely deafness occurred once and for all during the attack of cerebrospinal meningitis. He did not think the hearing was improvable—he must learn lip-reading.

The PRESIDENT said he did not doubt that the boy could hear somewhat at present, though he was becoming worse. The tympanic membranes seemed to him to be in-drawn. Some allowance must be made for the exaggeration of parents in their anxiety to persuade themselves that progress was being made.

Dr. DAN MCKENZIE did not regard the child as impenetrably deaf, as his mother could make him hear, and had taught him to say some words, although the deafness had come on before the speech period.

Dr. URBAN PRITCHARD said he did not agree with the second paragraph of the notes, because if a trained teacher were engaged to live with the child, that would be very effectual. He did not regard the child as so backward as the notes suggested.

Dr. H. J. DAVIS, in reply, said that by progressive deafness he meant that the hearing had slowly deteriorated, but not in the sense that it was oto-sclerosis. He believed the labyrinth was not destroyed at the time of illness, for the mother said he was now worse than before, and this was so. When one was speaking the boy looked intently at the speaker's face.



Here in England one had to wait so long before being able to send such a case to a suitable special school, whereas in America and other countries there was a properly organized scheme admitting of instant education to children, however young.

### **Sudden Deafness following Scald to Membrana Tympani by Steam.**

By H. J. DAVIS, M.B.

THE patient, a manageress in a laundry, aged 29, removed the lid off a cauldron. The steam escaped into her face, she turned her head sideways to avoid it, and at once felt acute pain in the ear and became "stone deaf" on that side. She was transferred to me from the Casualty department, and though locally there was nothing visible beyond blebs on the membrane and an exfoliating meatus, the hearing on that side was lost to the whole range of forks. The membrane never perforated, and as the acute symptoms subsided hearing was restored and is now normal.

The case is of interest as showing sudden and complete loss of audition resulting from a mere superficial inflammation of the membrane.

#### **DISCUSSION.**

Mr. CHEATLE said he assumed that "stone deaf" was the patient's own expression. He had seen one case in a lady who was carrying a kettle full of boiling water upstairs when she tripped, and some of the water entered her ear and burned a hole in her membrane. Her hearing, subsequently, became normal.

The PRESIDENT considered that there was a large psychical element in this case, as in cases of hysterical deafness following shocks.

Mr. WESTMACOTT said that he had recently seen a case of simulated deafness in connexion with the Workmen's Compensation Act. It was that of a weaver who was working at a loom when she fell, and was said to have run a pointed instrument, for picking up cotton, into the ear and perforated the drum, causing her to be stone deaf. A fortnight after the accident, when he saw her, there was a small punctured wound in the posterior wall of the meatus only, and not far from the orifice. Testing with Bárány's noise apparatus, however, revealed that there was no deafness at all.

**Deafness in a Case of Myxœdema.**

By H. J. DAVIS, M.B.

THE case exhibited is one of three cases (unfortunately the other two I have been unable to communicate with) of myxœdema in women, presenting all the classical signs of the disease well marked, so these need not therefore be referred to. In each instance they came to the Aural department first, as "they had come about their hearing." Their condition was obvious, and they were treated with thyroid extract, 5 gr., twice daily to commence with. In all there was marked improvement in hearing *pari passu* with improvement in general condition. The patient exhibited, a woman, aged 47, I first saw in June, 1910, the tuning fork tests pointing to affection of middle ear. A watch was inaudible on contact; membrane thin and transparent. After four months' thyroid treatment she heard a watch at 6 in., and to all intents and purposes was so well that she discontinued treatment; as she dropped back so did the hearing, and this happened twice. I saw her last, after twelve months' absence, on February 14. She is now in the same state as when I first saw her—watch inaudible, Rinne negative.

Another point of interest in these cases is that audition is delayed—just as speech and movements are "deliberate" so is the hearing—e.g., when a vibrating fork is placed on the mastoid she may at first say she does not hear it, and a few seconds later she will say "Oh yes, I do." I have no doubt she will improve, as she has done before, with thyroid treatment alone.

The PRESIDENT said he had had two similar cases, and in both improvement followed the administration of thyroid extract. He thought there were two elements in the deafness in those cases; one was a narrowing of the Eustachian tube, and the other the slowness of cerebral functions associated with myxœdema, which added some "nerve-deafness" to the case. Probably this patient would improve while she continued thyroid treatment.

**Epithelioma of Middle Ear invading the Middle and Posterior Fossæ of the Skull in a Man, aged 56.**

By H. J. DAVIS, M.B.

THE case was exhibited previously at the meeting on November 15, 1912,<sup>1</sup> when all that was visible was a malignant polypus protruding from the meatus. Three operations have been performed. The patient cannot be now shown as he is in intense pain—he is really dying of “earache”—and is kept under the influence of opium in the form of ext. codeinæ,  $\frac{1}{4}$  gr. ter die.

Photographs showing protrusion of auricle and the growth fungating through the meatus are exhibited.

[*Addendum*.—The patient died on February 20, and specimens of the temporal bone and the brain are exhibited, showing (1) the nodular growth implicating the dura mater in the middle and posterior fossæ; (2) the left half of the brain, showing a temporo-sphenoidal abscess lying above the growth. This had ruptured, and the patient died from suppurative meningitis. The under surface of the brain is invaded by cancerous growth. Specimens in formalin.

Pathological report of swab from cerebral abscess: *In films*, a long Gram-positive streptococcus and a Gram-negative short bacillus. *On agar and blood serum*, a short Gram-negative, freely mobile bacillus was grown; this is probably *Bacillus coli*.]

DISCUSSION.

Dr. H. J. DAVIS, in answer to the President, said that the patient was relieved of pain when the wound was left open.

Mr. MARK HOVELL raised the question as to why patients in this condition should be allowed to suffer so much pain when they could have relief by morphia or other sedatives. He mentioned the case of a patient of a well-known London hospital physician who had malignant disease, and who was given doses of morphia, increasing as the disease progressed, until she was taking 30 to 40 gr. a day, and on her bad days 40 to 50 gr. She used to awake free from pain, be quite cheerful, and take her food well, and to the end her suffering was but slight, in consequence of the treatment adopted.

Dr. H. J. DAVIS, in reply, said that he supposed the pain was that due to tension consequent on expansion of bone, and to nerve irritation consequent on their implication.

<sup>1</sup> See *Proceedings*, p. 34.

## Otological Section.

April 18, 1913.

Dr. J. DUNDAS GRANT, President of the Section, in the Chair.

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### Discussion on Functional and Simulated Affections of the Auditory Apparatus.

Opened by T. MARK HOVELL, F.R.C.S.Ed.

ON looking into the literature in connexion with this subject it seems to me that such a discussion as this is urgently needed, for the knowledge relating to this class of disorder appears to be more rudimentary, and appropriate treatment less clearly defined, than in connexion with most other aural affections.

The looseness of the phraseology in describing the disease is an indication that it has not received serious attention. It is frequently called "functional deafness" and "hysterical deafness," and the term "hysterical" in connexion with it is frequent.

Function is the office of any particular part of animal bodies, the peculiar or appropriate action of a member or part of the body, by which the animal economy is carried on. Thus we speak of the functions of the brain and nerves, of the heart, of the liver, of the muscles, &c. The *animal functions* are the motions, operations, or acts, which the organs, or system of organs, are fitted by Nature to perform; the proper action of the mechanism. Now the function of the ear is to hear, and deafness is therefore loss of function. This being the case, deafness cannot be functional.

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**CORRIGENDA.**—(1) In the report of Mr. Cheate's "Examination of both Temporal Bones" (February meeting), *Proceedings*, p. 59, line 10, the hyphen in "twenty-seven" should be omitted; the sentence should read: "Of these twenty, seven were so asymmetrical," &c. (2) In the same report, p. 60, line 1, for "Lenval Prize" read "Adam Politzer Prize."

## 74 *Functional and Simulated Affections of Auditory Apparatus*

The word hysterical, as you all know, is derived from *ὑστέρα*, a womb, but what has this organ to do with deafness? Granular pharyngitis is frequently caused by displacement of the uterus, as proved by the granulations disappearing without treatment when the womb is replaced in its normal position, but the affection is nevertheless properly called granular pharyngitis, as it is also produced by many other causes. The term "hysterical," however, frequently occurs in connexion with the subject under discussion, and the term "hysterical paralysis of the auditory nerve" is also used, which, taken literally, is farcical. Has not the time come when our profession, at any rate, should base nomenclature on ætiology?

Cases of the description under discussion most frequently occur in those individuals who wish to be exempted from military service, or who hope to obtain pecuniary advantage from the simulated disablement which is attributed to accident or other cause. There are, however, cases in which the hearing power appears to be suppressed as the result of a violent emotional influence, and others in which deafness is simulated without an apparent object, or in which the loss of hearing power cannot be explained otherwise than by a temporary want of the necessary nerve power or stimulus.

Sir William Dalby related a case<sup>1</sup> in which a girl, aged 17, came down in the morning apparently totally deaf, although from the unaltered modulations of her voice he felt certain that she possessed hearing power. Neurasthenic aphonia often occurs at the commencement of a menstrual period, and it would be interesting if it had been stated whether the simulated deafness occurred at this time. Six months later she came down to breakfast hearing quite well.

Dr. Ransom<sup>2</sup> mentions the case of a miner, aged 19, who awoke apparently unable to hear or utter a sound. He gave no sign when a cannon was fired close to him, stated by his father without the lad seeing or knowing it was about to be fired. He neither talked, whispered, nor uttered any inarticulate noises. His intellectual faculties were unimpaired, and he communicated by reading and writing. He was stated to have previously slept rather badly and to have complained of some pain in the occipital region and in the temples, otherwise his general condition seemed normal. He promptly did whatever he was told to do in writing, except that apparently he could

<sup>1</sup> *Brit. Med. Journ.*, 1895, i, p. 574.

<sup>2</sup> *Brit. Med. Journ.*, 1895, i, p. 470.

not repeat a word spoken to him or read aloud what he clearly understood or had himself written. Moderate pain did not produce any cry. A fortnight later—the symptoms having remained unchanged, he showed also anæsthesia of the palate and loss of the palate reflex, and the sudden movement of a hand before his eyes failed to make him blink. A faradic current was sent through the larynx by means of an intralaryngeal electrode and one on the front of the neck, the result being a kick and a yell. He was then told he could speak, and at once answered, "Yes, I can." The next morning he could answer questions uttered in a whisper. He went home hearing and speaking normally after having been deaf and dumb for five weeks.

Charcot, in his lectures, points out that the character of the deafness was quite unlike that of a malingerer, for he never started at the slightest noise made unexpectedly behind his back, whereas he did seem occasionally to comprehend simple orders made before his face, such orders being those that the doctor might be expected to give. A malingerer would have done the reverse. He also states that a malingerer would probably not feign loss of speech as well as loss of hearing, and anæsthesia of the palate could not be counterfeited by one ignorant of the symptoms of organic disease.

In another case mentioned by Dr. Van Dyck,<sup>1</sup> which occurred in a lad, aged 19, there was a history of masturbation, which would account for an exhausted condition of the nervous system. In this case it was stated that it had been noticed that the hearing had been apparently dull and that he had been unusually silent for the last two or three days, also that the deafness and speechlessness had been variable but had on the whole increased, until towards the close of the day in question it was found impossible to make the boy utter a sound or give evidence of hearing anything. He complained of having felt somewhat giddy for the last two or three days and that his ears felt stopped up, and he simply could not speak. He made hardly any attempt to communicate with anyone by signs or gestures, until when some words written proved illegible he would point to them and shake his head. He paid no heed to a loud shout and a sharp whistle or banging noise behind him, and wrote that he heard nothing. When the request was made by Dr. Van Dyck to a bystander in an ordinary tone of voice to have a bo'sun's whistle blown behind the boy's back suddenly, and he was asked after it had been done whether he had heard anything, he wrote, "I hear

<sup>1</sup> *Brit. Med. Journ.*, 1895, i, p. 973.

something like a whistle." Telling him to walk across the room, Dr. Van Dyck called loudly "Now, come back," expecting that one of the men standing by would turn him, but he turned of his own accord, and another order loudly and clearly uttered was promptly obeyed. Dr. Van Dyck now remarked in a loudish tone, "You hear me now," and the boy nodded. When asked his name he shook his head, and when asked to say one, two and three, he opened his mouth and made two or three feeble and utterly soundless efforts, and then shook his head again. When told to say "ah," after an apparent effort he got out a whispered and only just audible "ah," and with other words merely produced a sort of whispered stutter. When seen the next day he was hearing and speaking normally.

Here is the case of a lad with his nervous system presumably enfeebled by masturbation, and who gradually becomes less and less attentive to what is said to him, and who exhibits a diminishing effort to converse with those around him. May not this condition be due to an exhausted nervous system, not actually to deafness, but to blunted sensibility from nerve exhaustion, with no fixed wish to deceive, but an exaggerated condition of what most of us would feel when extremely tired, a feeling that one cannot be bothered to give the necessary attention to a matter, and that it must either wait or go?

In dealing with a case of deafness which is stated to be simulated, care must be taken not to be prejudiced by statements made by persons associated with the patient, and in all cases in which there is no apparent motive for loss of hearing it is desirable to remove the patient from uncongenial surroundings. The investigation should be undertaken carefully and thoroughly with a view to discovering diseased conditions if present. It must not be forgotten that in a large number of the cases in which deafness is simulated for advantage, there is a history of well-established impairment of hearing in one or both ears, and an examination clearly shows old-standing disease. The deafness therefore simulated is merely an additional degree. Each meatus and tympanic membrane should be carefully examined, and the possibility of the tympanum being full of fluid not forgotten, its presence usually being easily detected by the increased lustre of the membrane, even if a dark line marking the upper surface of the fluid is not visible. However, the injection of air into the tympanum by a Politzer's inflation, or through a catheter whilst listening with an auscultation tube to its entrance, will easily determine its existence or otherwise. The patency of the Eustachian tubes should be tested, and a careful inspection made of the nose and nasopharynx, fauces, &c.



In many cases of simulated deafness onset is sudden, and is stated to be discovered whilst the patient is alone, as on awaking in the morning. The modulations of the voice remain unaltered, and there is an absence of the quick movement of the eyes exhibited by most deaf persons to obtain the knowledge which normally they would derive by the sense of hearing.

Care should be taken that the tests employed to form a diagnosis are not of a nature which can do harm to the patient. I have been much struck in perusing the literature in connexion with this subject, to see how frequently guns and pistols have been fired, or proposed to be fired close to the patient, a procedure which, in my opinion, is not free from the risk of doing permanent injury to the patient's hearing, especially when the weapon had been fired, as has been done and proposed, in a confined space such as a room. In connexion with this it may be mentioned that should injury be done to the patient by such a method, it is possible that damages might be claimed against the investigator.

In cases in which there is no apparent reason for the simulation, recovery may sometimes be considerably hastened by the medical attendant behaving as though he considers the condition genuine, and not mentioning his opinion even to the friends, unless feeling sure that they can be trusted to act as though they held the same view. The statement made in a conversational tone of voice to the friends in the presence of the patient, that in such cases the hearing often returns as suddenly as it has gone, and therefore they need not be surprised if in this instance it is restored quite suddenly, will often have a beneficial effect, whereas if the patient thinks that malingering is suspected, the simulation may be maintained in order to prove that such is not the case.

Expressing sympathy with the manner in which the patient is afflicted, and carrying on a conversation on these lines with the friends whilst the examination of the patient is being conducted, and then asking the patient to put out the tongue or some request of that kind, will sometimes lead to the request being acceded to, the patient having been thrown off his guard by the apparently serious and sympathetic manner in which the examination was being conducted. Many malingerers have been detected by this method, but when it is a case where there is no apparent reason for the simulation, it is often advisable to make no comment on the return of the hearing power beyond satisfaction at the discomfort being no longer present.

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Dullness of hearing is more frequently simulated than absolute deafness, and, as before mentioned, in some cases the present condition assumed is merely an exaggeration of an old defect. A large number of tests have been employed with a view to ascertain to what extent a patient could hear, or to trick a supposed malingerer into giving an answer which would expose his deception. The following are amongst those considered most satisfactory. For unilateral deafness, supposed to be simulated, the following test should be applied: A plug of cotton-wool is inserted into the meatus of the normal ear and a vibrating tuning fork is then placed on the vertex. An impostor will probably assert that he does not hear the sound at all, whereas perception must be decidedly increased in the occluded ear. He may, on the other hand, admit that he hears the sound, though very faintly, on the deaf side. A plug of cotton-wool should now be placed in that ear; the sound ought to be strengthened, and the assertion that it is no longer heard will be proof of the imposition.

The watch and speech may next be used as tests, and the following plan will serve to detect imposition: The eyes are covered with a bandage, and the hearing distance for the sound ear is carefully determined. A plug of cotton-wool is then inserted into this ear, but not closely packed. When tested as before by means of the watch and speech, an impostor will probably assert that he hears nothing, whereas the insertion of cotton-wool into the meatus affects but slightly the hearing distance of a normal ear for speech. Words uttered with a moderate degree of loudness can still be heard at a distance of several yards. This test may be modified as follows: The examiner explains that he wishes to introduce an india-rubber plug into the sound ear; but he uses a piece of india-rubber tubing, which fits the meatus accurately, or a plug furnished with a stopper, which is withdrawn after insertion. Little if any, difference will thus be effected in the hearing power; but an impostor is likely to assert that his hearing is greatly impaired, or perhaps quite abolished.

The voice may also be utilized as a test in this way: The distance is ascertained at which spoken words can be clearly heard. The person's eyes are then bandaged, and the examiner retires to a greater distance, and utters words with the same degree of intensity. He then tests the hearing at various distances, some within and some beyond the normal distances. An impostor will get confused, and will probably assert that he fails to hear words uttered close to his ear, whilst those spoken at a much greater distance are admitted to be audible. There is yet another

plan : The examiner, remaining in the same spot, repeats a word several times, gradually lowering his voice.

A method devised by Teuber is very efficacious, but requires a special form of apparatus. The wall of a room is perforated by two metallic tubes, each of which is prolonged by a piece of india-rubber tubing. The latter terminates in an ear-piece for each meatus. Each india-rubber tube has a lateral branch, which is inserted into the meatus of an assistant. The examiner, who is out of sight, speaks first into one and then into the other tube : the words of sentences are of course heard by one or other assistant. If he makes rapid changes from one tube to the other, an impostor will soon get confused, and will fail to distinguish words spoken in one ear from those spoken in the other. When told to repeat what he has heard, he will prove that the ear which he declares to be deaf is capable of discharging its functions.

There is another and more simple method, based on the same principle. A tube is inserted into each ear; the examiner speaks through one, and his assistant through the other at the same time. In a genuine case the patient will repeat only what has been spoken into the normal ear; an impostor will become confused, and will repeat words heard on the side on which he asserts that he is deaf.

A binaural stethoscope may be utilized for detecting feigned unilateral deafness. In a case in which it was tried the patient asserted that he was deaf on the left side. A tightly fitting wooden plug was inserted into the right rubber tube and both rubber tubes were placed in the metal ones. Testing the instrument on himself, the examiner found that speech was not heard by the right ear. When the patient was thus tested he repeated without hesitation words spoken into the funnel-shaped end of the instrument which served as the mouthpiece. The tube containing the plug was then withdrawn from the right meatus, which was firmly closed by pressure on the tragus. On again speaking into the stethoscope, which was still connected with the left ear, the patient positively asserted that he heard nothing. He was conscious that the tube through which he had (as he supposed) before heard was no longer connected with the right ear.

For the detection of simulated bilateral deafness a bandage should be placed over the eyes, and each ear tested separately by speech and the acoumeter, the patient's statements being carefully noted with a view to discover contradictions. For the detection of simulated total deafness the person must be seen when asleep, and the amount of noise required to rouse him should then be noticed. If placed under

chloroform, so as to become only partially insensible, an impostor may answer questions put to him, or show by some remark that he hears the conversation that is going on around him. It has been suggested that during the ordinary examination a third person should make some disparaging or insulting observations with reference to the suspected impostor, while the examiner notices whether any effect is produced upon the features of the latter. Another suggestion of a similar character is that the examiner should tell the person that he may go, that he is unfit for work, &c. Such plans, however, would fail to detect a clever impostor, who would be quite prepared for any such attempts to throw him off his guard.

There is another method which by some is considered of use. It is employed as follows: The subject under investigation, with his clothes on, is stroked on the back alternately with a hand and with a brush, and after that the back is stroked with the hand whilst the physician's sleeve is simultaneously stroked with the brush. If the patient is really deaf, he will correctly answer whether his clothes are being stroked with a hand or a brush, as during these operations he solely trusts to his sense of feeling. The malingerer, on the other hand, will contradict himself in his replies, as in his case the perception of hearing is mixed up with that of feeling, and he does not know exactly whether he perceives the contact of the hand or brush, the noise of which he hears.

The PRESIDENT (Dr. J. Dundas Grant) demonstrated a case bearing on the subject of the discussion—namely, that of a woman, aged 29, unmarried, who complained of deafness, worse on the left side, which came on suddenly, three and a half weeks previously, after a "fit." The "fit" might be regarded as a vertiginous attack, but questioning brought out the probability that it was cardiac syncope. She was said to have been unconscious for several hours after the fit, and there was probably an hysterical element in the case. She had not experienced another fit, but her head occasionally became dizzy. There had been no vomiting. Since the attack she had been very deaf. The tuning-fork tests showed diminution of bone-conduction, and Rinne was positive in both ears; the deafness was therefore of nerve origin. On the right side she heard a whisper 4 in. away, but on the left she could not hear one in contact. Galton's whistle she heard at the mark 3·4 on the right side, 3·2 on the left. Her pharyngeal reflex was diminished, her knee-jerks increased; occasionally she had nystagmus, to left or

right, according to the direction of turning the eyes. On walking with the eyes shut, she deviated to the left. The voice-raising test with Bárány's "noise-machine" gave a very slight positive result. An interesting feature was that after a considerable amount of examination, including post-rhinoscopy, she seemed to "thaw" gradually, and certainly heard a little better at the end of the interview than at the beginning. When shown the hearing had greatly increased. It seemed to be entirely a neurosis. She was to have had the caloric test applied, but by the time the apparatus was ready she had left.

The President said that in the course of his experience he had seen a certain number of cases, and he considered that the one he had just exhibited was a genuine instance of functional deafness; there was an emotional, and possibly an hysterical element in it. She suffered from heart disease, and was consequently in a weak state nervously, and her circulation was defective. Her attack of syncope had scared her. There seemed to have been almost absolute deafness, but she recovered on her sensations being awakened in another direction. The diminution of the pharyngeal reflex was a sign of partial anæsthesia, though the case showed no actual hemianæsthesia.

Among the cases which had come under his notice was one of a worker in construction of a tunnel under the Thames. Many of the workers on that undertaking suffered from caisson disease, and they were somewhat well compensated for their deafness. This man came to him at the Central London Throat Hospital with what was considered to be unilateral deafness. The tuning fork on the vertex was better heard in the good ear; and when the good ear was stopped up, he professed not to hear at all. This profession was still kept up when the good ear was stopped, not with a solid plug, but with a hollow tube. He (Dr. Grant) was able to write to the doctor describing these observations, which gave him the information required.

A case of pure hysterical deafness was that of a young girl, whose nerve deafness was equal for all parts of the scale, and she was absolutely deaf for conversation. He thought one of the best proofs of the genuineness of deafness was the fact that a patient unwittingly acquired lip-reading; and this patient did. In her case he tried various methods of treatment, but nothing did her any good; later she was taken seriously ill, and this illness so completely altered her feelings, that she woke up one morning hearing quite well. Such cases became more clear if we adopted the idea that the patient was the subject of self-hypnotism; and the exhibitor understood that such people were not good subjects for hypnosis practised by another person.

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Another evidence of the reality of deafness was that of the "noise-machine," which he had just demonstrated on a patient. The reflexes sometimes indicated that the patient was hearing. A shrill whistle blown in the neighbourhood of the ear produced dilatation of the pupil if the patient did not know it was to be blown; he had found that useful in cases of deaf-mutism. In the case mentioned by Mr. Hovell, where the patient turned round when requested, he thought that was possibly an instance of the spell being broken during the course of the examination.

A case which had been under him for some time he considered to be merely functional. But on further examination he found that improvement was not taking place, and it appeared that the attack of deafness came on during severe neuritis affecting the side of the head, and that might have included the auditory nerve.

A case which was instructive to him occurred while pilocarpin was the vogue. A girl was sent from the country to the Throat and Ear Hospital as being absolutely deaf. Every case of nerve deafness was then thought to be suitable for pilocarpin, and she had injections of this every morning. On the second morning she began to hear a little of the traffic in the road, and on the third morning she heard well, and went home that day as a wonderful cure by pilocarpin. It was purely functional or simulated deafness.

Simulation did not confine itself to deafness; he had seen simulation of suppurative ear disease. In one such patient there appeared to be cheesy-looking material, and extraction and investigation proved it to be actually cheese. Another case was one of hæmorrhage from the ear in a girl at school. There was no evidence of erosion or ulcer from which the blood could come, but she had a carious molar tooth, with a polypus in it, and the slightest suction produced copious bleeding. She soaked handkerchiefs, and admitted that she did not like school.

A very interesting case was one of a poor lodging-house drudge who had come into the hospital and undergone a radical mastoid operation; after her dismissal she returned complaining of pain over the mastoid wound from which a small scrap of bone was seen projecting; this was extracted and though a very exceptional occurrence, was allowed to pass at the time. When, however, the following week she returned with another loose piece of bone in the same position, it became obvious that the occurrence was not a genuine one. She was therefore ordered at once into the hospital, and while she was having her preliminary bath the matron investigated her garments and belongings and found that



the poor creature was armed with a bone from a joint, from which she broke off the small scraps which she inserted into the mastoid wound. This pitiful endeavour to obtain respite from the drudgery of her everyday existence made her an object for commiseration rather than for blame.

He agreed with Mr. Hovell's advice not to be too ready to assume a case to be simulated, because he had been given infinite trouble through letting the patient see that was his view. One must be prepared to meet neuromimetics, but many cases one could not be quite sure about. When the tests were somewhat incongruous, it was probable that the case was functional, and especially if the dullness for high and for low tones was equal. As Mr. Hovell had so shrewdly indicated, the friends should be carefully told that "these cases sometimes get well as quickly as they come on." Sometimes that recovery ensued when some unorthodox or fanciful treatment was applied, just because the spell was broken.

He had listened with interest to Mr. Hovell's opening paper, and the Section was indebted to him for the trouble he had taken in introducing the subject.

Dr. W. MILLIGAN said the subject was of great interest, more especially from the medico-legal point of view. No doubt many of the members had been consulted in cases in regard to which questions of law might arise. His experience was that such cases were very difficult to unravel. He was surprised that Mr. Hovell had not enumerated in some detail some of the more modern tests, such as the vestibular reactions, the caloric tests, &c., which were of great use in differentiating functional from organic disease. It was difficult to know how exactly to regard hysteria. Was it a disease, or not? He had found great help from the vestibular reactions in cases of doubt, for in hysteria they were quite different from those met with in organic disease. As Dr. Dan McKenzie had published work on that subject he (the speaker) would not dilate upon it. But in what was regarded as hysteria, the vestibular reactions were all up and down, and they were not alike on separate examinations. The same might be said of the vertiginous symptoms. His experience had been that the simulated or functional diseases of the ear were mainly in the class of internal ear diseases. It was very seldom that one met with simulated affections of the external auditory apparatus. A very important point arose in the case of a person who had had disease in the external or middle ear beforehand,



and on the top of that simulated an increase of his trouble. Such cases were very difficult. The question of whether the patient was going to get damages or not had much to do with some of these cases getting well or otherwise. One case was that of a gentleman who was driving across a Yorkshire moor on a high dog-cart, and alleged he had been attacked and shot at by a neighbouring landlord, as a result of which he had lost his hearing, some pellets having entered his face. He (Dr. Milligan) could find no evidence of this. Feeling sure it was simulated deafness, he advised his counsel to get the matter settled out of court, and that he should get some damages, because he was wounded in other parts of the body. As soon as he got his damages his hearing returned. Simulation of deafness was more often on one side than on both, and required great care in its elucidation. The hints Mr. Hovell gave were very useful, and he endorsed what that gentleman said as to the inadvisability of firing a revolver near the patient, for damage might ensue, and a possibly functional condition be converted into an organic one.

Dr. MACNAUGHTON-JONES said, as the President had called upon him, the only short contribution he would make to the discussion would be to the references made by speakers to hysteria in its relation to functional affections of the auditory nerve. He did not like the term "hysterical deafness," and he agreed with what Mr. Hovell had said on that point. To him (Dr. Macnaughton-Jones) hysteria stood out as a distinct condition and a definite entity, with well-defined nervous phenomena and physical signs, quite apart from either neurasthenia or psychasthenia. In the nerve fatigue of neurasthenia the auditory nerve sometimes participated. When there was a typical psychical mental condition superadded to the fatigue, and when more manifest brain fatigue was present, we had to deal with psychasthenia, and here also one met with true functional auditory affections. He knew of no term in the whole of medicine which was more casually and crudely applied than that of hysteria. For his part, he did not think that he had ever seen a case of deafness that he would define as one of true hysteria. Nearly all the cases of functional trouble which he had come across, and in many of which nerve fatigue was present, were shown, not so much in deafness, as in other affections of the auditory apparatus. For instance, we saw it in hyperaesthesia acoustica, in which condition the sufferer could not live in a house with a piano, so great was the degree of auditory hypersensitiveness, and the striking of some particular note or chord caused a

painful sensation. He had seen some very startling recoveries from nervous conditions, such as that referred to by Dr. Milligan after railway accidents. He had known a man lame before verdict walk perfectly well a few days after it had been given in his favour. Many of these functional ear conditions were associated with weak heart and alterations in blood-pressure, and there was an undoubted connexion between the cardiac and the aural conditions. He once knew a case of functional deafness which was associated with inability to stand, and which threatened rather serious consequences to the person affected. The deafness and staggering gait passed off the same day. It had followed on an unusually large dose (30 gr.) of quinine which had been taken previously.

Dr. PEGLER said he had not heard any mention during the discussion of functional affections involving one ear only, nor whether the condition was much associated with tinnitus. He had recently seen a lady with unilateral deafness associated with tinnitus, which was probably functional. In her right ear she complained of sounds like the rushing of water down a weir. She had lived for twelve years in a house near a large weir, sleeping in a room much exposed to the noise of the water. Heard watch  $\frac{1}{2}$  in., conversation 2 yards. The treatment consisted in regular catheterization with medicated vapour under pressure, and vibratory massage of the tympanic membrane, combined with hydrobromic acid and strychnine. Removal to another residence completed the cure.

It was well known that in persons predisposed to nervous affections, constant exposure to the noise of the sea induced tinnitus and even deafness, of the same character as this patient suffered from.

Mr. MACLEOD YEARSLEY related the case of a malingerer whom it was very difficult to catch with the recognized tests. Finally, he retired with the other surgeons to a far part of the room while the subject was getting ready to go, and he (Mr. Yearsley) told them in an ordinary low voice funny stories, watching the man's face meanwhile. The man was quite unable to restrain his laughter, though it was patent that for some time he had been making great efforts to control his muscles.

Dr. DAN MCKENZIE said he considered that in organic deafness, particularly in old-standing cases, there was an element of functional

disability. The nerve-centres, not being exposed to the usual stimulus, fell asleep, as it were, and this functional element intensified the amount of deafness. It was to this fact, probably, that the success of those forms of treating deafness by means of musical noises was to be attributed; that the noises aroused the nerve-centres and rendered them more acute by re-educating them. Other methods of treatment which were successful in some people's hands exclusively, also owed their success to this fact in all probability. And he sometimes went so far as to think that paracusis Willisii might be due to a similar condition, and that the patient heard better in a noise because of the greater keenness of perception of the nerve-centre after it had been aroused from its apathy. With regard to the presence of functional disability in an organic case, he had a case, which he saw some time ago, in a lady who was absolutely deaf to all sound save thunder, and had conversed on her fingers for twenty years, yet her bone-conduction for the tuning fork over the mastoid was increased. One did not find such severe deafness from middle-ear disease alone, consequently the case must have been one in which the deafness was to a great extent purely functional.

Mr. HUGH JONES said he had thought there was often an added element of functional deafness, not only in cases of chronic deafness, but in more or less recent deafness in children and adolescents of degenerate type. Besides the well-recognized stigmata of degeneracy in the nasopharynx and palate it was possible that there was an epithelial change in the nerve apparatus, somewhat comparable to that seen in the teeth, crystalline lens, and other epiblastic tissues, which accounted for much of the deafness which one found it difficult to label and which made such individuals peculiarly liable to functional deafness.

Mr. MARK HOVELL, in reply, said he did not agree with the President that in one of the cases he referred to, the deafness was due to self-hypnosis, but rather thought it to be due to nerve exhaustion following masturbation. Some of the difficulties in hearing he attributed to the patient getting into a condition in which no attempt was made to listen; it might be called a disuse apathy. He agreed that he might have added to his paper the tests which Dr. Milligan laid stress on, and he had been much interested in Mr. Yearsley's instance of taking the subject off his guard. But of course he had not attempted to enumerate all the tests which could be applied.

## Otological Section.

May 16, 1913.

Dr. J. DUNDAS GRANT, President of the Section, in the Chair.

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### Unilateral Deformity of the Ear with Obliterated Meatus in a Child, aged 8 ; Internal Ear Normal.

By E. A. PETERS, M.D.

PATIENT, G. H., was born with a deformed ear. The mother cannot assign a maternal impression. The helix and anti-helix are fused and small. The tragus and anti-tragus are relatively diminished in size, while the cartilage is flat, small, with definite edges. There is no evidence of the presence of muscle, and the external auditory meatus is represented by a shallow pit.

Tests (Weber) referred to right : Contact, no loss ; watch,  $\frac{8}{60}$  ; tuning fork, 126 on mastoid, no loss.

### Post-mortem Specimen of Unilateral Deformity of the Auricle, Meatus, and Middle Ear.

By E. D. DAVIS, F.R.C.S.

THE specimen was obtained, by the aid of Dr. S. Fouracre, from a child aged 8 months, who died from enteritis and convulsions. There is no family history of deformities. The auricle is undeveloped, and no signs of cartilaginous or bony meatus existed, but a blood-vessel occupied the position of the meatus. The middle ear is filled with gelatinous embryonic tissue in which fairly developed malleus and incus are embedded. The Eustachian tube is represented by a fissure, which is difficult to find. The internal ear has not been minutely dissected. The auditory nerve and brain appeared to be normal ; the latter has been sent to Dr. Mott for investigation.

A skiagram was taken during life, but was useless.

## DISCUSSION.

Dr. DONELAN asked as to the mental history of Dr. Peters's case on the mother's side, because deformities of the ear were found in many cases where there had been insanity in the family, and the descendance, he believed, was generally from mother to son.

Mr. MACLEOD YEARSLEY said that a case was published by Melland,<sup>1</sup> of deformity of the ear, in which a maternal impression was attributed as the cause of the deformity. But it appeared that the mother saw the deformity of ear in only the last six weeks of her pregnancy, and as the ear was completely developed by about the end of the third month that impression could not have been the cause. He believed it had been said that in all cases like the present there was loss of bone-conduction. He had not found that to be so: many of the cases of deformity of ear which he had seen agreed with the present case.

Dr. PETERS replied that he had hoped to hear whether it was wise to do a modified mastoid operation, with skin-grafting, and whether such a procedure would be likely to be followed by improved hearing. With regard to Mr. E. D. Davis's specimen, he had seen two or three cases with deformed external ears and apparent deafness in the first year of life, when, though the skiagrapher was uncertain as to the presence of an internal ear, partial hearing had developed in the second year. In this case either the partial hearing explained the afferent delay of a functioning ear, or it was possible that the tympanum was filled with embryonic rather than pathological tissue as in Mr. Davis's case. The infantile condition generally disappeared with development of hearing.

The PRESIDENT (Dr. Dundas Grant) said the question which arose was whether some good could have been done by operation in Mr. Davis's case; the middle ear seemed as if it might have been a useful one, though there was very little room for getting at it by operation. The literature showed that there had been many operative failures in these cases; and apparently in only one, by Vali, of Budapest, was great perseverance at last rewarded by success.

**Epithelioma of the Helix in a Man, aged 70.**

By H. J. DAVIS, M.B.

THE situation of the ulcer on the edge of the helix is interesting, and it was first mistaken for a Hunterian sore, but no glands were involved and a Wassermann reaction was negative. Ten weeks before admission, on March 11, the patient, a country gardener, "noticed

<sup>1</sup> *Brit. Journ. Child. Dis.*, 1908, v, p. 481.

a hard, painless lump on the edge of the ear." "It broke and developed into a sore." This was followed by neuralgia over the parietal region. The edges of the sore were everted and very hard. The ulcer was 1 in. long by  $\frac{1}{2}$  in. wide. I removed a piece of the edge of the ulcer, and it was reported as epithelioma. The auricle was then amputated. The area of attachment of the pinna to the side of the head is larger than one would suppose, as the accompanying photograph indicates. No grafting was necessary as the raw surface epithelialized with astonishing rapidity. A tube has been worn in the meatus to obviate contracture. The patient is quite well and has gained weight since the removal of the pinna.



FIG. 1.

Fig. 1.—Epithelioma of helix. Ten weeks' growth.



FIG. 2.

Fig. 2.—Showing size of granulating surface fourteen days after the auricle was removed. A tube is worn in the meatus to obviate contraction.

### DISCUSSION.

Dr. W. MILLIGAN congratulated Dr. Davis on the excellent result, and suggested that an artificial ear should be procured for the patient. It could be obtained from Mr. Brooke, of Halifax, Yorks. He asked whether there had been a history of injury in the case as an exciting cause. He was interested in the question of injury as an aetiological factor in the development of carcinoma, and some years ago he showed two cases before the Society, where in both there had been injury to the margin of the helix and epithelioma had developed subsequently. One otological authority said that the upper third of the margin of the helix was the usual situation for the development of epithelioma, on account of the sparse circulation.

Mr. SYDNEY SCOTT asked whether Dr. Davis proposed to remove the cervical and pre-auricular glands, or whether he intended to wait until their obvious enlargement indicated this necessity. He suggested anticipating further trouble by removal of those glands now.

Dr. DAN MCKENZIE said he showed some years ago at the old British Laryngological Association,<sup>1</sup> a case of epithelioma of the pinna in an old man, aged 75. There the disease began at the back of the pinna, not at the edge. He removed the auricle, as Dr. Davis had done in this case, and with, at first, a pleasing result. But before the lapse of many months there was recurrence of the disease in the scar, and the man died of it. In the discussion on the case at the Association, someone suggested that it might have been advisable partially to close the raw area left after the removal of the pinna, by splitting the lobule and turning it up as a flap.

The PRESIDENT said he had shown a similar case in which the epithelioma was in the upper third. In that case he removed a wedge, fairly wide of the epithelioma, and the patient lived many years after the operation without recurrence and without enlargement of glands. He asked whether Mr. Scott had invariably found involvement of glands after complete removal of the pinna. Possibly the wedge operation was the preferable one.

Mr. SYME said he had had a case under care in which there was epithelioma of the upper part of the auricle. It commenced as a small pimple and had been constantly picked. He did a wedge operation, but, unfortunately, it did not include removal of glands, which were not then palpable. But there was a recurrence in the glands with very rapid enlargement. He had never seen such an acute recurrence. The patient was a man aged 90.

Mr. COLLEDGE said he had seen a case of malignant disease of one ear on which operation was done by the late Mr. Clinton Dent in 1905—namely, removal of a wedge only. The patient returned to hospital last year (1912) with a similar condition in the other ear. There was no sign of recurrence on the side previously operated upon, although the glands had not been touched.

Dr. H. J. DAVIS, in reply, thanked Dr. Milligan for his information concerning an artificial ear. There was no history of injury in the case, except the usual ear-boxing which everyone experienced at school. Mr. Scott's suggestion was in his mind when he operated, but as the glands were not enlarged he decided to do nothing further. At the present time there was no indication of any glandular involvement. The case was a very early one.

<sup>1</sup> *Journ. Laryngol.*, 1906, xxi, p. 105.



**Occlusion of the Meatus and Middle Ear by Bone following Operation for Acute Mastoiditis and Extradural Abscess.**

By H. J. DAVIS, M.B.

In October, 1912, the patient, a boy, aged 10, was operated on twice for extensive mastoid disease—a large abscess in the posterior fossa was dealt with at the same time. A radical mastoid was completed at the



Skiagram (by Dr. Morton) showing excess of new bone formation. The arrow indicates the position of the internal auditory meatus.

second operation when the post-aural wound was closed by a plastic operation. The boy had facial paralysis, which is improving with electrical treatment. The patient, who had been very ill, recovered and left the hospital for a convalescent home in December, 1912. It will be observed that the large bone cavity is now not only completely filled in, but the process of new bone formation has extended and entirely occluded the meatus; presumably the mastoid, middle ear, and meatus are converted into a mass of solid bone. The usual difficulty

experienced after extensive bone operations in this region is to heal or obliterate the cavity left after operation, but this has occurred in this case by an over-extension of the normal process of bone repair. Whether the present state of things is an advantage to the patient or not is questionable ; at all events the ear is "dry" and there is no disease.

#### DISCUSSION.

The PRESIDENT said that he had from time to time found, on opening such a case again, that he seemed not to have cleared away the bone as freely as he ought to have done, though at the time he thought he was very thorough : it looked as if some fresh development of bone had taken place. Such a condition was probably more frequent than was generally supposed.

Dr. W. MILLIGAN asked whether it was not really a question of sepsis, in which a hyperostosis was produced as the result of a still-continuing septic process. He believed the ear was still discharging, and he did not think the disease had disappeared. One sometimes saw such a condition where sepsis remained at the bottom of the cavity.

Dr. H. J. DAVIS replied that the ear had been dry for six months until three days ago, when it recommenced discharging through the minutest pin-point hole in the meatus. The skiagram report was that the meatus was only partially occluded by bone. But what the radiographer took to be the external auditory meatus was probably the internal meatus. There was much new bone formation, and if that could be depended on as a result in every case, it would be a great gain in the cases where the difficulty was to fill up large spaces in the bone left after operation.

#### **Persistent Paroxysmal Cough apparently due to Irritation of Chorda Tympani Nerve by a Spicule of Steel which penetrated the Tympanum.**

By JAMES DONELAN, M.B.

THE patient, a man, aged 45, was sent to Dr. Donelan six years ago by Dr. Cassidi, of Derby. Some days after visiting the engineering works of the Midland Railway Company he was attacked by a violent fit of coughing with feeling of discomfort along the left side of the tongue. This symptom constantly recurred on apparently no provocation from any ascertainable cause for two years. His larynx, except for a general hyperæmia, probably due to the cough, was normal. Nothing could be found in the cervical or thoracic regions that accounted

for it. He had been repeatedly examined by various medical authorities. Dr. Donelan made a similar examination without result until he inspected the ears as part of a routine method. The right ear, meatus and tympanum were normal. So were the left, except for a tiny black spot with a reddish areola round it. This was situated just behind the malleus at exactly the spot where the chorda tympani nerve crosses it. Cocaine was applied, and a small spicule of steel about 3 mm. long was extracted. The patient had a most violent fit of coughing then, but according to the last report of Dr. Cassidi a few months ago he has had no further return of his trouble.

Dr. Donelan was wishful at the time to bring this case to the notice of the then Otological Society, but being unable to secure the attendance of the patient, he thought he was thereby debarred from doing so. He has only just learned that such is no longer the case.

### **Congenital Prominent Auricles treated by Operation.**

By J. DUNDAS GRANT, M.D., and DAN MCKENZIE, M.D.

The patient is a lad, aged 10. Three years ago his mother brought him to the Central Throat and Ear Hospital on account of his "ugly



I.

II.

Prominent auricles treated by operation. On the left side a portion of the auricular cartilage was removed. The second photograph was taken three years after operation.

ears." They were, indeed, very unsightly, as the photograph, taken before operation, shows the whole auricular cartilage standing out from the head like the ears of a bat. The left auricle in addition to its outward projection showed also a downward droop. Dr. Grant operated on the left ear, and Dr. Dan McKenzie on the right. In the case of the left ear the skin of the posterior surfaces of the auricle and of the adjoining portion of the mastoid region was removed, and in addition a narrow segment of the auricular cartilage involving its whole thickness and traversing the anti-helix was excised in order to hinder the resiliency of the cartilage from restoring the prominence of the auricle after operation. In the right ear, the operator contented himself with rawing the skin surface. The cartilage on this side was not excised or cut through. The result, on both sides, proved satisfactory. The auricles are now closely applied to the head; but the case undoubtedly shows the advantage of removing a slip of cartilage, as the left ear is now the less prominent of the two. As it is more than three years since the operation there is hope that the benefit may turn out to be permanent.

#### DISCUSSION.

The PRESIDENT said the question was whether it was advisable, in all cases of outstanding ears, to remove a portion of the cartilage at the same time. The side from which the cartilage was removed was a little closer, but the difference was not very great. It seemed that the right principle was to remove the cartilage in the worst cases, and in the slighter ones to try to do without that procedure.

Mr. WESTMACOTT said he had had several cases in which he had carried the operation wound farther back. There was a good deal of stretching when the ear bent so far forward; he always made the incision as far outwards as the ridge behind the edge of the pinna, removed the skin from the cartilage and also from the scalp for a similar area, and then laid the ear back against the head, suturing the edges. He had found this more successful in preventing recurrence of deformity. There was a sufficient sulcus left to keep spectacles in position if they need be worn.

Dr. H. J. DAVIS suggested that when such an operation was required on both ears the same surgeon should do the two operations, so as to ensure uniformity on the two sides. Here one ear was somewhat more prominent than its fellow. He knew of an instance in a boy who was operated upon when he was at a public school. One operation consisted in removing part of the helix, and on the other ear a posterior operation was performed; hence the asymmetry was as noticeable as before.

**Photographs of a Case of Congenital Prominent Auricles  
improved by Operation.**

By DAN MCKENZIE, M.D.

THE patient, a girl, was operated on at the age of 4. Result satisfactory.



I.

II.

Prominent auricles treated by operation; auricular cartilage not removed.  
Second photograph taken six months after operation.

**Thrombo-phlebitis of the Mastoid Emissary Vein.**

By DAN MCKENZIE, M.D.

THE patient, a little boy, aged 8, was operated on for acute mastoiditis, on March 18, 1913, at the Ilford Emergency Hospital. The mastoid cells were found to extend farther back than could be comfortably reached through the post-aural incision, and so the usual incision running horizontally backwards from the middle of the post-aural incision was made. In so doing a large vessel was cut and spouted very freely. In the absence of antiseptic wax (soap or paraffin might have taken its place!) the bleeding was after a time arrested by the pressure of a gauze tampon plugged into what turned out to be

the foramen of an unusually capacious mastoid emissary vein. The operation was then concluded in the usual way. Three days after operation the temperature rose to 102.2° F., falling to 99° F. in the evening. Next day a similar rise was recorded, and on March 22, suspecting the onset of thrombosis of the lateral sinus, I re-opened the wound and exposed the mastoid emissary vein lying in a bony canal about  $\frac{1}{2}$  in. in length. The vein was turgid and sausage-looking, and so large that at first sight I mistook it for the lateral sinus. On being slit up the vein was found to contain a blood-clot about  $\frac{1}{4}$  in. in length; and the vessel itself was seen to be about as wide as a large goose-quill. After the clot was shelled out of the vein regurgitant bleeding took place from the lateral sinus, and an extension of the incision into the walls of the sinus showed the latter vessel to be healthy. Thirty-six hours after the operation the temperature fell to normal, and it has remained normal ever since.

#### DISCUSSION.

Dr. W. MILLIGAN said that if one had not got antiseptic wax at hand, a very good substitute was to take a wooden match, sterilize it, whittle it down and insert it into the bone at the bleeding point, or the point of a Krause's hook might be inserted into the bleeding point, and so twisted about as to cause the blood-vessel to contract.

Dr. MCKENZIE said he did not think that a match whittled down would have been large enough in this case, as it was a very large vein.

#### Case of Congenital Syphilitic Deafness treated by Neo-salvarsan.

By JOHN F. O'MALLEY, F.R.C.S.

E. W., AGED 10, came under my care in the aural department at St. Bartholomew's Hospital on December 16, 1912, with a history of one year's deafness on both sides. There was also a history of earache three weeks before, together with sore throat and nasal discharge, which had lasted for three days, and for this she was referred to Mr. W. D. Harmer, who reported: "Both antra are quite clear to transillumination; no discharge seen." The tympanic membranes were retracted, Rinne negative, and this, with the history, pointed to chronic Eustachian catarrh as the cause of deafness; but the combination of the more

complete function tests raised sufficient doubt to induce me to have a Wassermann reaction taken, although the patient had none of the commoner stigmata of congenital specific disease.

December 16, 1912: Function tests:—

|   |     |                 |     |     | Right                    |     | Left     |
|---|-----|-----------------|-----|-----|--------------------------|-----|----------|
| Acoumeter   | ... | ...             | ... | ... | 3 ft.                    | ... | 2 ft.    |
| Whisper   | {   | Numbers         | ... | ... | 9 "                      | ... | 6 to 9 " |
|   |     | Sentences, some | ... | ... | 7 "                      | ... | 6 "      |
|   |     | " others        | ... | ... | 4 "                      | ... | 2 "      |
| C <sub>2</sub> fork—  |     |                 |     |     |                          |     |          |
| Rinne   | ... | ...             | ... | ... | Negative                 | ... | Negative |
| A. B. C. (absolute bone-conduction, fork on mastoid, meatus closed) | ... | ...             | ... | ... | — 30                     | ... | — 35     |
| C <sub>4</sub> (air-conduction)                                     | ... | ...             | ... | ... | $\frac{5}{17}$ of normal | ... | —        |
| Wassermann negative.  |     |                 |     |     |                          |     |          |

December 23, 1912: Wassermann positive.

January 13, 1913: 0.3 grm. of neo-salvarsan intravenously.

February 17, 1913: 0.3 grm. of neo-salvarsan intravenously.

March 10, 1913: Whisper test for sentences went up to 18 ft.

March 17, 1913: 0.3 neo-salvarsan.

March 19, 1913: Wassermann negative.

April 16, 1913: Function tests:—

|                                 |     |     |     |     | Right                   |     | Left     |
|---------------------------------|-----|-----|-----|-----|-------------------------|-----|----------|
| Acoumeter                       | ... | ... | ... | ... | 22 ft.                  | ... | 14 ft.   |
| Whisper, sentences, various     | ... | ... | ... | ... | 21 "                    | ... | 21 "     |
| C <sub>2</sub> Rinne            | ... | ... | ... | ... | Positive                | ... | Positive |
| A. B. C....                     | ... | ... | ... | ... | — 15                    | ... | — 15     |
| C <sub>4</sub> (air-conduction) | ... | ... | ... | ... | $\frac{1}{4}$ of normal | ... | —        |

For permission to show this case I am indebted to Mr. C. E. West, who has also kindly verified the diagnosis and some of the tests.

## DISCUSSION.

The PRESIDENT said the bone-conduction tests seemed to be conclusive, and the Wassermann reaction confirmed the history, but the physiognomy did not give support to the idea of syphilis, so it was important the Wassermann test was made.

Dr. DAN MCKENZIE said Mr. Beddoes had asked him to put two questions to Mr. O'Malley: (1) What was his reason for using neo-salvarsan? (2) Had mercury been used?

Dr. W. MILLIGAN did not feel certain that it was a syphilitic ear case, and there was ambiguity about some of the tests. It might have been a case of panotitis following influenza in a syphilitic subject. There was clinical evidence of there having been a recent middle-ear lesion with tubal obstruction.



Mr. E. D. DAVIS said he had used neo-salvarsan in several cases, though in only one ear case, and he used it because it was so easily dissolved in distilled water. With salvarsan it was quite a process to prepare it, having first to neutralize the alkali and then neutralize the acid. Moreover, the results seemed just as good as with salvarsan.

Mr. WHALE did not agree with Mr. Edward Davis's remark; he had several times given from nine to fifteen doses of neo-salvarsan before the Wassermann became negative, and that was a serious drawback in treatment.

Mr. SYDNEY SCOTT said it was very important to be sure whether this was really so-called congenital syphilitic deafness. The patient probably had had syphilis, as the Wassermann was positive and he was deaf, but it did not follow that the deafness was due to the syphilis. The tests pointed to the existence of Eustachian catarrh, and he strongly deprecated the conclusion that it was definitely a case of syphilitic deafness cured by neo-salvarsan.

The PRESIDENT said it would be inadvisable to use salvarsan in any case unless one was sure it was syphilitic. The drug had not been entirely acquitted of causing arsenical disturbances in the nervous system.

Mr. O'MALLEY replied that the neo-salvarsan was supplied to the department because it was easier to use. No mercury had been given to the patient. With regard to Eustachian catarrh, he had reported the case exactly as it came to him, and Mr. West agreed with the diagnosis and congratulated him on the result. Her deafness was a year old, and she had to be placed on the front seat in her class. It was that fact, coupled with marked shortening of bone conduction, which led him to have the Wassermann done. After three doses the hearing strikingly improved. He was a sceptic as to improvement following treatment, and allowed for contributory factors, such as the expectations of the patient, and the observer's own hopes. It was only because the results of the tests were so striking that he submitted the case for Mr. West's judgment, which agreed with his own.

### A Case of Phlebitis without Thrombosis of the Sigmoid Sinus.

By ARTHUR CHEATLE, F.R.C.S.

A CHILD, aged 1 year and 11 months, was admitted to King's College Hospital on March 11, 1913, acutely ill with a mastoid abscess and a temperature of 103° F. At the operation on the same day it was found that the sigmoid sinus had been exposed by the disease. The sinus wall did not appear to be granulating, but felt and looked quite smooth,

and appeared firm. The next afternoon as the child was not relieved, and the temperature in the morning was  $104\frac{1}{2}^{\circ}$  F. (without a rigor), the sinus was very thoroughly exposed; it appeared pale and "lumpy," and felt firm. On incising it no blood escaped. The jugular vein, which was collapsed and not thrombosed down to the combined facial and lingual, was then tied and divided. The sinus being thoroughly opened, it was then found that the firm feeling was due to great thickening of the wall, and that the lumen was exceedingly small and contained a little fluid blood without any thrombus. No flow of blood could be obtained even when a curette was passed nearly up to the torcular. No bacteriological examination of the sinus blood was made, as cessation of breathing occurred and the operation had to be finished in a hurry. The child was rather ill for four days, but after that recovery was quick and uneventful. The condition appears to have been one of inflammation of the sinus wall, and it is a question whether free exposure alone would not have sufficed.

**Acute Suppuration of the Middle Ear with Postero-superior  
Bulging, treated by means of Hartmann's Punch Forceps;  
Rapid Subsidence.**

By J. DUNDAS GRANT, M.D.

L. G. HAD an attack of influenza about six weeks ago, which was followed by acute inflammation of the right middle ear. There was a rounded swelling filling the fundus, formed no doubt by a bulging of the postero-superior part of the membrane, bathed in pus; after clearance of the moisture and the application of cocaine, a narrow crescent of normal tympanic membrane could be seen on pushing up the bulging portion of the membrane. Puncturing with a paracentesis needle would not have been sufficient for drainage, as the swelling was not a simple sac of thin membrane, but was apparently chiefly inflammatory tissue; a more useful opening was therefore made by punching out a small piece with Hartmann's small aural punch forceps. The perforation healed, and the hearing returned completely in about three weeks after this was done. There is now a slight depression behind the handle of the malleus. (This use of Hartmann's forceps was advocated at the Boston International Otolological Congress by Dr. Lewis.)

**Narrowing after Radical Mastoid Operation treated by means  
of Hartmann's Punch Forceps.**

By J. DUNDAS GRANT, M.D.

THE patient, a girl, aged 12, had had a radical mastoid operation performed, but the ear did not get well, and she came under the exhibitor's care for other reasons. He found an oozing from the ear and at the site of the operation a diaphragm over the deeper part of the operation cavity with a very small opening in it, scarcely larger than a pin-hole. One disadvantage of the minuteness of the opening was that the antiseptic drops could not obtain entrance. He cocainized the ear and introduced a probe covered with cotton-wool and dilated the hole sufficiently to allow of the introduction of Hartmann's punch forceps (with the points turning upwards). With that he cut upwards and punched out a portion of the diaphragm; the opening was now about 4 mm. across, and on looking through it granulations could be seen; some of these he had removed with the punch forceps and a cutting ring, and in addition he had on several occasions injected a few drops of a 1 per cent. solution of chloride of zinc up the Eustachian tube. The ear was now doing well, and re-opening of the mastoid cavity had been avoided.

**Chronic Attic Suppuration treated by Operation with Retention  
of Ossicles and Remains of Membrane.**

By J. DUNDAS GRANT, M.D.

MISS A., aged 23, had had discharge from her left ear for about ten years. The discharge issued from the attic, there being no perforation in the lower part of the membrane and no perforation sound on inflation; the hearing was very good (better than it would be after the complete mastoid operation). The exhibitor, therefore, performed the mastoid operation, retaining the ossicles and as much of the tympanic membrane as remained, and taking away the overhanging bone over the cavity from which the pus came. The diseased cavity was there-

fore shut off from the Eustachian tube and the nasopharynx, and healing took place extremely quickly. If the ossicles and membrane had been removed and the cavity of disease had been left in communication with the pharynx, then the slightest cold in the nasopharynx would have extended up into the tympanum and delayed the healing, from the continuous slight reinfection. The discharge has stopped for some weeks and there is now an opening into the aditus and antrum, the edges of which are still stained red by the scarlet-red ointment.

The PRESIDENT, in answer to Dr. Syme, said that the attic was removed ten weeks ago.

**Chronic Suppuration of the Middle Ear, rebellious to Trans-meatal Treatment until supplemented by Tubal Injections of Chloride of Zinc.**

By J. DUNDAS GRANT, M.D.

Miss D. O., aged 20, first seen on February 11, 1913, on account of discharge from her right ear, which had lasted on and off since childhood, and had been worse during the last eighteen months; the lower portion of the tympanic membrane was absent. The condition failed to respond to simple treatment, such as cleansing and the instillation of spirit drops through the meatus, and the question arose as to whether a radical mastoid operation would be necessary. However, the exhibitor decided to continue with the spirit drops a little longer, and in addition, at first twice a week, and then once, he injected a few drops of a 1 per cent. solution of chloride of zinc up the Eustachian tube through the Eustachian catheter; a little cocaine was first sprayed up the Eustachian catheter, then the chloride of zinc was blown in, and finally a few drops of paroleine were injected in order to drive the chloride of zinc right up into the tympanum. Speedy improvement ensued and at present there is no sign of pus.

**Temporo-sphenoidal Abscess following Mastoid Disease and Aural Polypus.**

By H. J. DAVIS, M.B.

THE patient, a girl, aged 14, was admitted to the hospital six weeks ago with vomiting, vertigo, and facial paralysis. A large aural polypus was protruding from the meatus. There had been otorrhea on and off for four years. There was no indication of any mastoid tenderness. The polypus was removed and the mastoid antrum opened; the roof of the antrum was eroded and an extradural abscess was evacuated. The brain protruded into the wound, but did not pulsate; a knife was therefore passed into the temporo-sphenoidal lobe, and 3 drachms of pus evacuated. The dura mater was snipped away over the brain abscess area, and the wound left open. The girl has made an uninterrupted recovery and is now well.

**Drawing and Description of a Double Skin-flap in the Radical Mastoid Operation.**

By P. WATSON-WILLIAMS, M.D.

FIRST incision extends from just above the highest point of attachment of the pinna, curving outwards and backwards well within the margin of the hairy scalp, curving forwards below to the mastoid tip. The skin and soft tissues are dissected forwards to the margin of the bony meatus, leaving the periosteum. The posterior meatal cartilage (with skin) is divided by a longitudinal incision extending into the meatus (fig. 1), and the auricle and skin-flap are held forward together, while with a narrow knife two incisions are made extending from the tympanic ring so as to divide the posterior cartilaginous and membranous meatus above and below. The higher incision is extended upwards, and the lower one horizontally backwards on the mastoid eminence. The periosteum is raised from the bone together with the attached posterior meatal wall (fig. 2), much as in Hugh Jones's method, and turned backwards and upwards till the bone operation is completed, when it is replaced so as to form a periosteal lining to the upper and back part of the bone cavity. The lower flap of periosteum is also



FIG. 1.

Skin-flap dissected forwards as far as the margin of bony meatus, periosteum left intact; an incision has been made into the meatus, dividing the posterior meatal cartilage from the auricle.

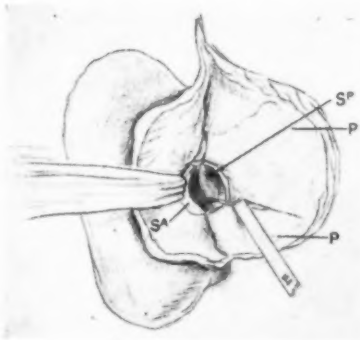


FIG. 2.

Fig. 2.—The posterior meatal cartilage and skin (Sp) has been divided from the rest by an upper and lower incision, and the periosteum (P) also shows the two incisions—one horizontal, the other nearly vertical. A periosteal elevator is being inserted beneath the periosteum and meatal flap. Sa, the anterior part of the cartilaginous meatus, exposed to view.

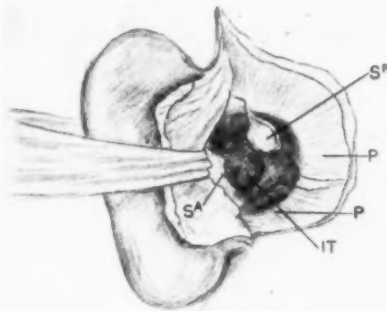


FIG. 3.

Fig. 3.—The mastoid operation has been performed and the periosteal-meatal skin-flap (Sp) replaced in position so as to line the upper and back part of the bone cavity, where it is retained in contact with the bone by the subsequent packing. P, P, the upper and lower periosteum flaps. Sa, the anterior undisturbed meatal wall, exposed by drawing forward the auricle, &c. IT, inner tympanic wall.

replaced and the conchal flap is then formed (Milligan's flap) and is secured by a catgut ligature. The meatal skin-flap then lines, with the periosteum, the upper and back part of the bone cavity (fig. 3), while the conchal skin-flap lines the floor and inner aspect of the auricle where it overlies the bone cavity. The inner tympanic wall in cases where useful hearing exists can usually be retained intact, only the orifice of the Eustachian tube and hypotympanum being curetted. The infected tympanic wall mucosa recovers, much as the mucosa lining a maxillary antrum in antral suppuration, and in many favourable cases the patient may thus be left with good hearing power.

By the double skin-flap here described one combines the advantages of Hugh Jones's flap (*vide* vol. vi, No. 2, p. 22) with that described by the author as a periosteal lining flap (*vide* vol. vi, No. 5, p. 61), and appeared to promote rapid epithelialization of the mastoid cavity in the author's experience of the few cases in which the double skin-flap was used.

### Post-mortem Specimen of a Radical Mastoid Operation performed Six Months before Death.

By E. D. DAVIS, F.R.C.S.

THE patient was a comedian, who had suffered for some years from pulmonary tuberculosis. During sanatorium treatment he developed mastoiditis and facial paralysis, following chronic otorrhœa. At the time of the radical mastoid operation he was suffering from advanced laryngeal and pulmonary tuberculosis. The mastoid process was extensively involved, and in removing the focus of disease a large area of the dura mater of the middle fossa was exposed. The post-aural wound healed by first intention, and the patient left the hospital after ten days with the symptoms relieved and health improved. When seen about six months before death, the mastoid cavity was satisfactory.

The post-mortem showed extensive laryngeal, pulmonary and intestinal tuberculosis. The middle fossa dura mater was thickened and the exposed area covered by tuberculous granulation tissue. The petrous bone below the dura and surrounding the opening made at the operation was necrosed. The brain was normal, and the meninges, apart from those in immediate relation to the area of operation, were unaffected.



PROCEEDINGS  
OF THE  
ROYAL SOCIETY OF MEDICINE

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VOLUME THE SIXTH

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COMPRISING THE REPORT OF THE PROCEEDINGS FOR THE  
SESSION 1912-13

PATHOLOGICAL SECTION



LONDON  
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1913

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The Council think it right to state that the Society does not hold itself in any way responsible for the statements made or the views put forward in the various papers.

## Pathological Section.

October 15, 1912.

Dr. R. T. HEWLETT, President of the Section, in the Chair.

### The Microscopic Structure of Urate Calculi.

By S. G. SHATTOCK.

#### De structurâ penitiori calculorum ex salibus uraticis constantium.

##### SUMMARIUM.

QUOD structuram calculi ex acido urico constantes in duo genera dividi possunt; alii compacti, alii cancellati (vide vol. iv).

Calculi uratici, ex contrario, semper compacti sunt, et stratis superpositis aedificantur; radii crystalliformes absunt.

Calculorum, ammonii uratis, nucleus construitur de sphaerulis uraticis sine ordine aggregatis, et muco vesicali, credere licet, cohaerentibus.

Calculi corpus, extra nucleum, e sphaerulis oritur crescentibus sed imperfectis (hemisphaerulis vel conis) quae lateribus conjunctae laminae compactas formant.

Hemisphaerulae ipsique conis, ut sphaerulae perfectae, de crystallis minutissimis sive bacilliformibus, ut dicantur, construuntur: hi crystalli radialiter disponuntur, et lineis concentricis intersecantibus in zonulis dividuntur.

Laminae sic constructae oriri insuper possunt sine hemisphaerularum vel conorum conjunctione, hoc modo: crystalli bacilliformes magis ad calculi totius centrum diriguntur quam ad singula centra super calculum sparsa.

Hujus structurae interruptitur uniformitas depositione zonulari vel sphaerularum sine ordine aggregatarum, ut in nucleo, vel crystallorum

## 2 Shattock: *Microscopic Structure of Urate Calculi*

baeilliformum sine ordine iterum depositorum: ambo genera depositionis porro sociari possunt, sphaerulis et crystallis intermixtis.

Crystalli bacilliformes, etsi in calculis uraticis abundanter deponuntur, raro tamen, ut sedimentum in urinâ reperiuntur.

Ut in sedimentis sic in calculis, calcii uratis sphaerulae e crystallis longioribus constant quorum extremitates e margine projiciuntur.

In a previous communication<sup>1</sup> I have fully described and illustrated the microscopic structure of urinary calculi composed of uric acid, where I have also dealt with the general considerations attaching to the subject. The present communication may be taken, therefore, as a continuation of that already published. And in this, the microscopic structure of calculi composed of urate will be similarly detailed.

An inspection of any extensive collection of urinary calculi will show that the number consisting entirely of urate, as compared with those consisting entirely of uric acid, is strikingly small. At the time when Beale published his work on "Kidney Diseases and Urinary Deposits" (1869) there were in the extensive collection of the Royal College of Surgeons, 32.92 per cent. of calculi consisting entirely of uric acid; whilst those of urate were only 2.15 per cent., and of oxalate of lime 5.12 per cent. In the Norwich Hospital Museum the proportions were: Uric acid, 24.73 per cent.; urate, 8.29 per cent.; oxalate of lime, 3.16 per cent. In Guy's Hospital Museum they were: Uric acid, 15.38; urate, 3.84; oxalate, 9.13. Composite or alternating calculi of which the *nucleus* consists of urate, however, are less infrequent; they form nearly a third of the whole collection in the College.

One marked structural difference between the uric acid and urate series is, that whilst calculi of the former are crystalline, those of the latter are not; except with the reservation that, under a high power, material which appears at first sight to be structureless is in reality very finely crystalline. In their macroscopic characters, calculi of urate may be perfectly smooth exteriorly, or finely granular, or lowly tuberculated. The divided surface is lustreless, incapable of taking the high polish of uric acid, and of a light clay colour.

In the case of uric acid concretions, two well-marked forms occur: a compact and a cancellated. No corresponding difference is met with in urate. The urate calculus is invariably compact in section; it exhibits a fine concentric lamination, although this is not so pronounced

<sup>1</sup> *Proc. Roy. Soc. Med.*, 1911, iv (Path. Sect.), pp. 110-146.

as in the case of the compact uric acid forms. A certain number of narrow concentric fissures, incomplete in their circuit, occur in some calculi, but this has no proper resemblance to the definite arcade-like construction of cancellated uric acid. The radial striation which is sometimes evident in compact calculi of uric acid is absent in those of urate. As compared with the uric acid series, the variety of microscopic structure presented by the uratic is markedly less. The fundamental mode of construction is either an aggregation of spherules, of the kinds occurring in urinary sediments, or depositions having essentially the same minute structure, but extending round the entire circuit of the calculus.

I may now proceed to describe in detail a selection of typical specimens, and afterwards summarize their structure, and comment upon the data they present.

AMMONIUM URATE, B 12, ST. THOMAS'S HOSPITAL.

A smooth ovoidal calculus 1.8 cm. ( $\frac{7}{10}$  in.) in chief diameter. To the naked eye a minute nucleus was discernible in the hemisection during the process of grinding; this was of irregularly oval form, with a finely undulating margin.

*Microscopic Structure.*

*Nucleus.*—The section, which includes this in its entirety, shows it to be composed exclusively of closely aggregated spherules. The spherules are doubly striated, and polyhedral from mutual apposition; they present, that is, a fine radial striation, and a concentric marking due to the succession of clear structureless lines which intervene between the wider radially striated zones. In places, spheres occur in an almost isolated or discrete condition owing to the absence of others in juxtaposition, there being natural lacunæ in the otherwise compact structure. Some of these half-isolated spheres are of the typical hedgehog form, the sphere, which is itself sharply defined, being beset, yet not always densely, with radiating spicules. These details of structure indicate that the spheres have grown in a more or less free state before cohering to produce a proper nucleus. The edges of the spherules in general are frayed or actinate; and their component radial crystals are closer and finer in some than in others. The spheres themselves vary in magnitude. In those situations where such spheres are compacted there appears an intervening granular-looking line which results from



#### 4 Shattock: *Microscopic Structure of Urate Calculi*

their crystalline borders being viewed in optical section; the general appearance has a certain resemblance to that presented by the prickle cells in a section of the epidermis.

As regards the *body* of the calculus, this is constructed of a series of compact wavy zones, between which there occur belts of bacilliform urate, or of spheres aggregated without order, or of both combined. These intervening disorderly layers vary considerably in thickness in different parts of their circuit, and it is this irregularity which gives rise to the undulations of the more regularly and compactly constructed laminae. The compact zones, which vary individually in thickness, are subdivided concentrically; they are constructed, that is to say, of fine vertically (or radially) set bacilliform<sup>1</sup> crystals, separated into a subseries of concentric zones by fine and structureless horizontal lines. In short, such zones, which surround the entire calculus, repeat the construction of a single uratic sphere. These zones in some cases are deposited upon a subjacent series of spheres which lie in lateral apposition, or upon fan-shaped or cuneiform elements, which represent sectors of spheres, the structure of which they thus continue to extend, without any indication of their true origin remaining. In other cases this regularly laminated structure arises directly upon a zone of less regularly disposed bacilliform crystals. As before stated, there occur zones which are composed almost entirely of closely compacted spherules of mutually adapted forms, like those composing the nucleus. Individually, such a zone as traced round the calculus varies much in thickness, and it may be incomplete. In places the spherular aggregates are so local and prominent as almost to constitute secondary nuclei: over such the suprajacent zones are, for some distance, correspondingly elevated.

It is easy to understand from such a repetition of the nuclear structure, how other independent calculi may originate during the growth of the first. The lowly tuberculated or granular character of the exterior which some uratic calculi present, is due to the coarser or finer undulations produced by the localized elevations of spheres and bacilliform crystals already referred to. In this particular calculus there is, near the middle of the body, a narrow zone of clear, uncoloured crystalline material which completely encircles the section. That this consists of calcium oxalate is evident from its characters, which in every detail correspond with those constructing calculi composed chemically of this substance.<sup>2</sup> The zone is absolutely unpigmented, radially

<sup>1</sup> This term I use to indicate the minute size and general shape of the crystals.

<sup>2</sup> W. M. Ord and S. G. Shattock, *Trans. Path. Soc. Lond.*, 1895, xlvii, p. 91.

crystalline, and, in addition, marked by a fine circumferential or cross striation. In some parts of the narrow ring, the radially set crystals are individually discernible, and of tablet form; in others, they cohere into cones, or, as they appear in the sections, rosettes or fan-shaped structures. This zone of calcium oxalate is abruptly interposed in the midst of the urate. There is a second equally narrow zone of the same material nearer to, though still at some distance from, the nucleus.

It is of passing interest to observe that spontaneous fractures, accompanied with the loss of fragments, have occurred in the deeper part of the body of the calculus, the surface so deformed having been subsequently encrusted with the next succeeding deposit. And it is especially interesting to note that in each case, the deposition which follows, and which closes the fractured surface, whilst it at the same time encircles the undamaged part of the circumference, is the narrow zone of calcium oxalate already described. The fact suggests that some alteration in the character of the urine has been the immediate cause of the fracture, and supports the views originally put forward by Dr. W. M. Ord in connexion with the spontaneous fracture of calculi.

#### AMMONIUM URATE, B 17, ST. THOMAS'S HOSPITAL.

This calculus is of spheroidal form, 1 cm. ( $\frac{3}{8}$  in.) in diameter; its surface is lowly tuberoso, and is, in addition, finely, though not universally, tuberculated. Its section is of a uniformly dull, clay colour.

*Nucleus.*—In regard to the nucleus, this is constituted by closely compacted spherules of urate, the periphery of which is not sharply defined, but finely frayed and crystalline. The spherules are of irregular form from their growth having occurred whilst in juxtaposition, so that in the section they produce a complete mosaic; and they are of the simplest construction, consisting of fine, radially disposed bacilliform crystals. Complete spheres are uncommon, the crystalline body being frequently represented by a segment only of the sphere, so as to appear fan-shaped in the microscopic section.

*Body.*—The method in which the more differentiated substance of the "body" arises is by the more orderly arrangement, and lateral apposition, of spherules of a kind similar to some such as form the nucleus. The transition is not very abrupt and does not involve the entire circumference, but occurs in patches. The spheres, by the lateral apposition and cohesion of which the body takes its origin, are all incomplete, and appear in the section as fan-shaped structures. As

## EXPLANATION OF PLATE I.

FIG. 1 (B 12, Ammonium Urate, St. Thomas's Medical School).—A section made so as to include the entire nucleus with the surrounding portion of the body of the calculus. The nucleus, which is of irregular, somewhat lobulated outline, consists solely of an aggregate of spherules devoid of any arrangement, and presumably held together by vesical mucus. The succeeding laminated structure of the body is of the kind described under certain of the figures which follow. ( $\frac{3}{8}$  obj.)

FIG. 2 (B 12, Ammonium Urate, St. Thomas's Medical School).—Portion of the nucleus, which consists of an aggregate of spherules. Many of these are beset with somewhat coarse, slightly curved spines, the "hedgehog" spherules of urinary sediments. The intervals may have been artificially produced in grinding the specimen, or they may represent natural spaces once occupied by mucus. The way in which these delicate processes are retained intact indicates that the cohesion of the spherules was brought about by intervening vesical mucus. ( $\frac{1}{6}$  obj.)

FIG. 3 (B 9, Ammonium Urate, St. Thomas's Medical School).—Portion of the body of the calculus, showing four or five laminae of compact substance, marked by fine striæ concentric with the centre of the calculus; their radial striation is, in most, too delicate to be recognizable in the photograph. These laminae are separated by, and owe their undulations to, broad deposits which consist of collections of spherules of varying sizes, and polyhedral or incomplete from mutual apposition. In the case of the upper part of the third lamina from the bottom of the figure, an origin may be traced from the coalescence of the laterally apposed conoidal segments of spherules. In the highest lamina the formation has taken place without such coalescence, the substance consisting of bacilliform crystals radially disposed with regard to the centre of the calculus, and set immediately upon the zone beneath, which consists of spherules without any orderly disposition. ( $\frac{1}{6}$  obj.)

FIG. 4 (B 12, Ammonium Urate, St. Thomas's Medical School).—A section from the body of the calculus, showing the usual concentrically striated wavy zones of compact substance. The general structure is interrupted a short way below the centre of the field by the interposition of a somewhat broad, irregular zone of minute, bacilliform crystals without any orderly disposition, and in this respect differing from those which construct the compact laminae by their regular parallelism at right angles to the direction of the laminae themselves. Two or three similar, but interrupted zones of lesser breadth occur elsewhere. ( $\frac{1}{6}$  obj.)

FIG. 5 (Urate, probably of Ammonium).—Portion of the "body," a short distance beyond the proper nucleus, showing the inclusion of a second, microscopic calculus, after this has become adherent to what was at one time the growing surface. The calculus in question has a nucleus of uratic spherules, and consists, beyond this, of wavy concentric laminae and intercalated groups of spherules. ( $\frac{3}{8}$  obj.)

FIG. 6 (Bb 8, Ammonium Urate, with Alternating Calcium Oxalate, St. Thomas's Medical School).—Portion from the centre of the calculus, showing a piece of a second, fractured uratic calculus, which forms the nucleus of the concretion. (No calcium oxalate occurs in the field shown.) The proper calculus is the regularly laminated portion on the left-hand side, and above an artificial fissure which separates it from the fragment forming the nucleus. An inspection will show that the nucleus itself does not represent a simple fragment of another calculus, for it consists of a long triangular process comprising parts of two large spheres below, and a group of smaller spherules above; on the right-hand side of this fragment there is a regular laminated line of deposit, succeeded by broad zones of spherules and further laminae, which indicate that the triangular segment has served as the nucleus of a calculus which has again been fractured; one of the fragments of this has furnished the nucleus of the calculus depicted. ( $\frac{3}{8}$  obj.)

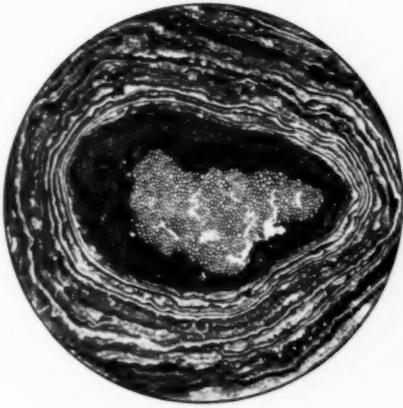


FIG. 1.

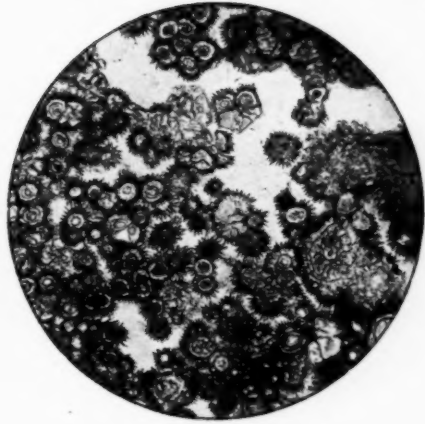


FIG. 2.



FIG. 3.

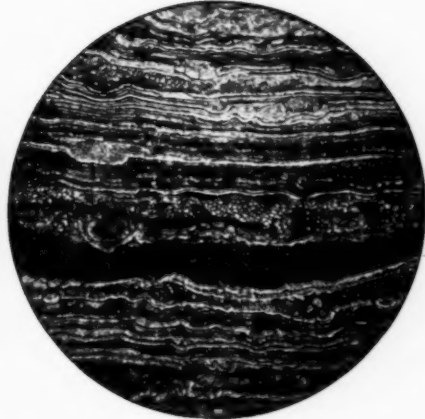


FIG. 4.

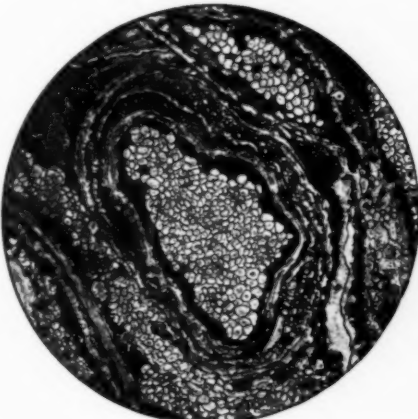


FIG. 5.



FIG. 6.



described in the preceding calculus, the zones so resulting are both radially and concentrically striated, the cross-striae of the adjacent cones being undulatory when viewed in continuity. In the case of other zones such a mode of origin does not obtain, the doubly striated material being devoid of undulations, and deposited directly upon the growing surface, as described in the foregoing specimen. The regular course of the laminae, all of which are compact, or without lacunae, is disturbed in places by hemi-elliptical aggregates of spherules of the same kind as those which construct the nucleus. The general laminae which immediately follow are continued over such aggregates, being correspondingly elevated, and thrown into undulations. In some cases such aggregations are really the nuclei of secondary calculi which have become adherent, and in course of time covered in and incorporated with the whole; these aggregations are individually surrounded by complete zones of doubly striated substance; concentric, that is, with the centre of each secondary calculus. Furthermore, there occur somewhat broad zones of varying thickness, composed of bacilliform crystals devoid of any kind of arrangement, radial or other; in such zones there may also occur intermingled and disorderly groups of spherules.

AMMONIUM URATE, B 9, ST. THOMAS'S HOSPITAL.

The exterior, to the naked eye, is finely, but not uniformly, granular. Microscopically, the *nucleus* is an aggregate of spherules.

The *body* is constructed in a manner practically identical with the two foregoing. It consists of compact, doubly striated zones of varying thickness, and rendered undulatory by the interposition of others which consist of finely crystalline urate, or of spheres without order, or of both these combined. These atypical zones, although they may be uninterrupted in circuit, vary considerably in thickness at different spots, and in this way give rise to conspicuous undulations in the overlying compact layers. The typical compact layers themselves arise, in some cases, by the lateral coalescence of doubly striated hemispheres, or lesser, conoidal sectors of spheres; in other cases they arise directly upon the subjacent surface.

AMMONIUM URATE, B 3, ST. THOMAS'S HOSPITAL.

Microscopically, the *nucleus* is an aggregate of doubly striated spheres, which construct a beautiful mosaic of polyhedral or mutually adapted elements. The spheres vary in size, and have a well-defined edge which is not frayed out by the projecting ends of the fine, radially

## 8 Shattock: *Microscopic Structure of Urate Calculi*

set crystals composing them. Bacilliform crystals occur intermingled with the spheres.

The *body* is built up in the same way as that already fully described in the foregoing specimens. It arises on the nucleus of spheres exactly as the more distal undulating zones arise upon the more circumferential layers of similar aggregates of spheres—viz., either by the lateral apposition and cohesion of doubly striated sectors of spheres, or by the direct formation of doubly striated zones, without sphere formation.

### AMMONIUM URATE, WITH ZONES OF CALCIUM OXALATE.

The *nucleus* consists of closely packed polyhedral spheres and intermingled bacilliform material.

Upon this the *body* arises by the lateral apposition and coalescence of sections of spheres. The compact, doubly striated zones of the body result—some from the cohesion of laterally apposed spheres or conoidal sectors of such, others from the close vertical, or radial, deposition of bacilliform crystals. Intercalated between regularly constructed zones of those kinds, there are others consisting of discrete spheres and intermixed bacilliform crystals, the irregularities in the thickness of such zones producing undulations in the succeeding deposition.

Incorporated in the body, in the vicinity of the nucleus, there are a certain number of secondary (microscopic) calculi. These have precisely the same structure, on a miniature scale, as the main concretion, and consist of a nucleus of aggregated spheres completely surrounded with compact wavy laminae. It is obvious that these cannot have been formed in situ, since the nucleus of each is *completely* encompassed by a compact periphery; they are evidently minute calculi of independent formation which have become adherent to the growing surface, and afterwards incorporated in the main structure.

Equally interesting is the interposition of uncoloured, transparent zones of calcium oxalate. The first of these appears as a narrow, interrupted belt of doubly striated cones, laterally apposed, and evidently growing side by side with the urate, since the uratic cones (or segments of spheres) directly fill the gaps between the others. The urate is doubly striated and typical in disposition. In the urate succeeding, isolated cones of oxalate are sparsely distributed without any order, and have been deposited side by side, and simultaneously, with the pigmented urate. To this succeeds a complete zone of typical calcium oxalate, then a narrow zone of urate, incomplete in its circuit; and beyond this, zones of urate and of oxalate alternate to the surface.



AMMONIUM URATE, FOLLOWED BY CALCIUM OXALATE,  
Bb 6, ST. THOMAS'S HOSPITAL.

The *body* presents the usual uratic structure. Zones of calcium oxalate are intercalated. These consist of laterally apposed, uncoloured, transparent, doubly striated cones. The zones may be incomplete; and moreover, isolated cones of oxalate may occur in the zones which are uratic. The oxalate increases in amount towards the exterior, and acquires the coarsely granular or mulberry surface during its growth, from the lateral coalescence of compound cones, or what are hemispheres or sectors of secondary calculi. Over such undulating surfaces looped or wavy lines of urate are deposited, to be succeeded by further formations of oxalate. In many instances these uratic interpositions consist solely of doubly striated, discrete, or uncoalesced, spheres, with intermingled bacilliform crystals.

The *nucleus* of this calculus consists of a fragment of a second, fractured uratic calculus constructed of doubly striated laminae and zones of spheres.

AMMONIUM URATE, FOLLOWED BY CALCIUM OXALATE,  
Bb 8, ST. THOMAS'S HOSPITAL.

The *nucleus* of this calculus is formed by one of the fragments of a second calculus which has undergone spontaneous fracture. The fragment in question is shoe-shaped, and its laminae are altogether different in course from those of the surrounding substance; some, indeed, abut at right angles to those which succeed them. Its structure is similar to that of calculi of ammonium urate in general. Beyond this central fragment, the proper calculus consists of regularly laminated substance and of zones of closely packed spheres. The laminar zones are doubly striated in the way already detailed under other specimens. In addition, there are intercalated zones of bacilliform crystals of the kind which construct the regular compact laminae, but in which the component crystals want the radial disposition, and exhibit no order whatever. At a distance from the centre, calcium oxalate is admixed with the urate. This occurs at first as transparent crystalline cones, either isolated, or laterally apposed in groups; at times the isolated deposit occurs in hemispheres or even in nearly complete rosettes. Farther outwards, zones of this material completely surround the concretion, the superficial portion consisting solely of oxalate, the free surface of which is highly granulated or lowly tubercular. In the

## EXPLANATION OF PLATE II.

FIG. 7 (Urate, probably of Ammonium, with alternating Calcium Oxalate).—Portion of the "body," showing the usual laminated structure of ammonium urate as described in preceding figures. In addition to this there are shown three zones of perfectly transparent calcium oxalate. These zones consist of the laterally coalesced conoidal segments of spherules, and exhibit a double striation—i.e., they have a delicate concentric marking, and a radial (not recognizable under the magnification shown), the latter indicating that they represent a fusion of fine, radially disposed crystals. In several spots, isolated cones of calcium oxalate occur; these have been formed on the growing surface synchronously with the uratic cones amidst which they lie. ( $\frac{3}{8}$  obj.)

FIG. 8 (Bb 6, Ammonium Urate and Calcium Oxalate, St. Thomas's Medical School).—Part of the "body" of the calculus, showing a growth of spherules of ammonium urate on what was at one time the free surface of the calculus. The calcium oxalate consists of doubly striated, transparent cones, coherent in lateral apposition. What was at one period the free surface upon which the urate has been deposited, is deeply cleft, or of the mulberry type. On this the urate has been laid in the form of incomplete spherules. At the upper limit of the urate a regular surface has resulted from the coalescence of the uratic hemispheres and cones. On the cessation of the uratic formation, the oxalate has again been deposited. There were several such narrow undulating lines of urate in the main mass comprising the body of the calculus. ( $\frac{1}{8}$  obj.)

FIG. 9 (A 126, Calcium Urate and Uric Acid, Royal College of Surgeons).—The calculus was formed around a bodkin which was introduced into the bladder. The section is from the immediate vicinity of the foreign body, and has an open, bone-like character, consisting of trabeculæ which are composed of closely adapted coherent spherules, of varying sizes, of calcium urate. The spherules, which, of course, are seen in section, have particularly jagged edges, and consist of radially disposed and very evident crystals; they are devoid of concentric markings. ( $\frac{3}{8}$  obj.)

FIG. 10 (A 126, Calcium Urate and Uric Acid, Royal College of Surgeons).—A portion of the same section as the preceding, more highly magnified. The coarsely crystalline, radial structure of the spherules is well shown, as well as their large size, and the way in which the free ends of the component crystals interdigitate with those of adjacent spherules. ( $\frac{1}{8}$  obj.)

FIG. 11 (A 64, Calcium Urate and Uric Acid, Royal College of Surgeons).—A section of the compact "body" of the calculus, showing coarsely crystalline spheres with jagged margins, consisting of calcium urate; associated with these there are a certain number of cuboidal crystals of uric acid such as occur in calculi of the last-named substance. ( $\frac{3}{8}$  obj.)

FIG. 12 (Urinary Sediment of Uric Acid).—Crystals, washed in distilled water, and treated with solution of caustic potash. The figure shows the organic matrix (mucin) which is brought into view by the solution of the uric acid. The matrix, which is slightly creased, is that of a barrel-shaped crystal, and that of a group of rhombs. ( $\frac{1}{8}$  obj.)



FIG. 7.

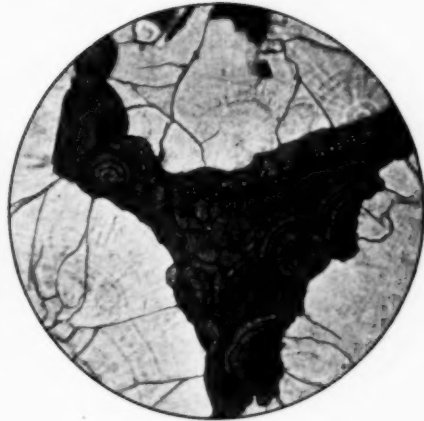


FIG. 8.

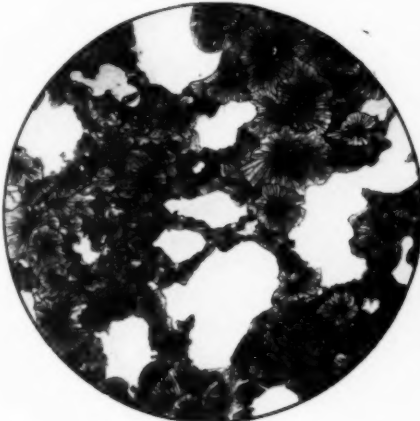


FIG. 9.



FIG. 10.



FIG. 11.

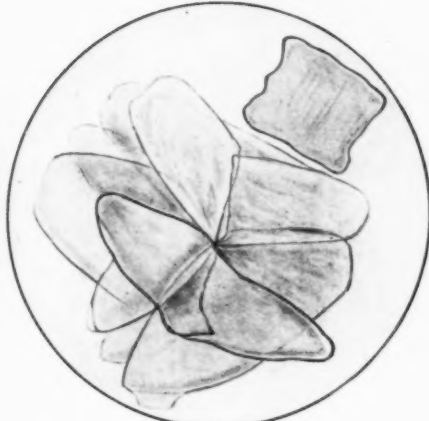
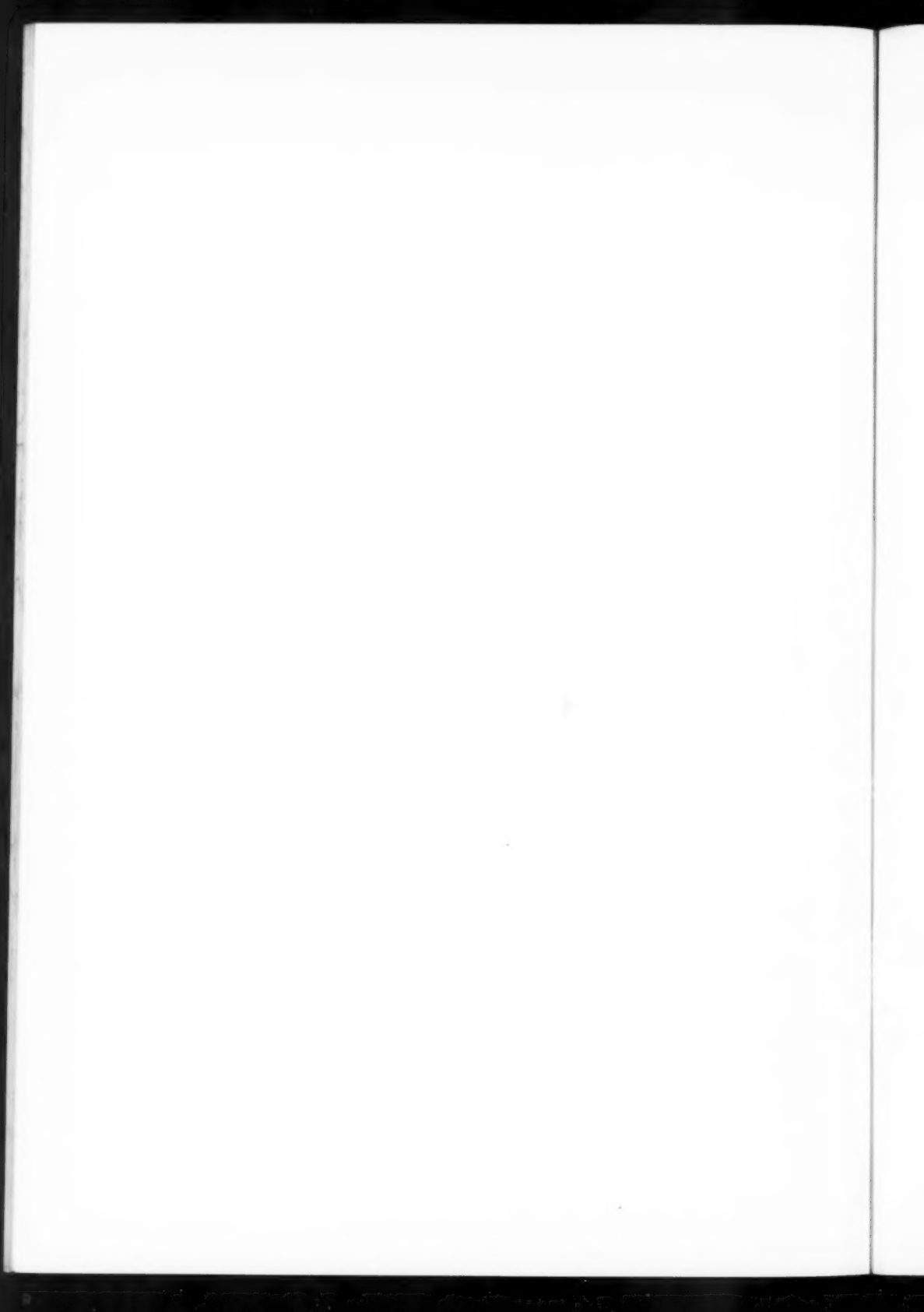


FIG. 12.



proper oxalate there occur stray groups of uratic spheres which are distinguished by their pale brownish-yellow colour, and want of perfect transparency; the radial striation of these is finer than that of the spherular oxalate.

CALCIUM URATE (IMPURE), A 126, ROYAL COLLEGE OF SURGEONS.

This is a calculus from the human bladder, which has a slender piece of steel for its *nucleus*. Chemically it consists of impure uric acid, with irregular layers and partial deposits of ammonium urate mixed with oxalate, and urate of calcium. The concretion is of the size and shape of a hen's egg; the needle which forms the nucleus lies centrally in its longer axis, although the deposition has accumulated more at one pole than at the other. The specimen was presented to the College by Sir William Blizard, and is figured in the College Catalogue of Calculi (pl. iv, fig. 6) as an extremely rare instance of the deposition of uric acid upon a foreign body. As studied in the divided surface, by the naked eye, it is of compact, laminated structure, except for a distance of about 6 mm. ( $\frac{1}{4}$  in.) around the included body, where the structure is of a closely cancellated kind. From one of the halves of this calculus I prepared a microscopic section, this being made so as to include the actual furrow in which the bodkin lay. The following microscopic description applies only to the portion in the neighbourhood of the nucleus, and which, as told by its minute structure, consists of calcium urate. In the microscopic section it is regularly cancellated, not unlike finely cancellous bone. The trabeculae consist of closely aggregated, radially striated spherules, with finely jagged or more deeply frayed edges. Many of the spheres are of conspicuous size and exhibit a particularly well pronounced radial striation indicative of their consisting of a crystalline aggregate. Although the trabeculae for some distance around the foreign body are disposed more or less at right angles to it, this is not due to a proper radial crystallization, for the columns, like the other trabeculae, are constructed solely of aggregated crystalline spheres. The free ends of the component crystals of the adjacent spheres interdigitate, so as to produce an intimately coherent structure. None of the spheres exhibit a concentric striation. These spheres correspond in every detail with those which occur in urinary sediments, and which consist chemically of calcium urate.<sup>1</sup> This calculus consists more outwardly of radially crystalline uric acid.

<sup>1</sup> Beale, "Kidney Diseases and Urinary Deposits," 1869, pl. v, fig. 3; Rieder and Delépine, "Atlas of Urinary Sediments," 1899.

## URIC ACID AND CALCIUM URATE, A 64, ROYAL COLLEGE OF SURGEONS.

A large, coarsely cancellated calculus. Microscopically it consists of spheres compactly set, but without any order, in coarse trabeculae, with comparatively small interspaces, much as in a section of bone. The spheres are of large size, with coarse radial markings, and frayed or jagged edges, by means of which they are closely interlocked; they are devoid of concentric striation. Their pale yellow colour is of itself sufficient to disprove their being of calcium oxalate. Although a zone may result from the lateral apposition of incomplete spheres—i.e., of hemispheres or of cones, there is no concentric striation in such a zone. In such zones, again, neither the outer nor the inner border is sharply defined or curvilinear, but irregular in correspondence with the jagged peripheral character of the cones. Farther from the centre the spheres are of smaller size, but compactly aggregated, with few or no interspaces. Only at a considerable distance does a laminated construction arise, and this is very imperfect, appearing at first in segments of the material in the general spherular conglomerate. Blocks of uric acid are distributed amongst the spheres; indeed, here and there, small aggregates of such blocks occur, with interspaces, as I have figured in my previous communication on the microscopic structure of uric acid calculi.<sup>1</sup> The purer portions of uric acid in this calculus need not be further referred to in connexion with the present subject.

In the College catalogue the calculus is placed in the uric acid series. The conclusion drawn from its microscopic structure, that it contains urate of lime, is corroborated by a further chemical examination, which was carried out by Mr. H. R. Le Sueur; this demonstrates the presence of an appreciable amount of calcium.

## POTASSIUM URATE, P 7, ROYAL COLLEGE OF SURGEONS.

No calculus composed of urate of potassium has been met with in the human subject. In the College collection, however, there are three calculi of magnitude, which consist wholly or chiefly of this salt. Two of them come from the Sloane Museum, and, as remarked in the College catalogue, all three are probably from the urinary bladder of some of the species of iguana found in South America.

<sup>1</sup> *Proc. Roy. Soc. Med.*, 1911, iv (Path. Sect.), pp. 110-146.

P 6: This calculus, which is the size of a hen's egg, was entitled in the Sloanian M.S. Catalogue "Pedra di Yguana," and consists of urate of potassium, ammonium, and calcium.

P 7: This calculus is composed, according to Taylor's analysis, of urate of potassium, and being well adapted for it, I prepared a microscopic section. It is an ovoidal concretion about the size of a pigeon's egg, with an almost smooth exterior. In section it is white, like one of the phosphatic group. Centrally it consists of a very friable, pure white, structureless material. This portion merges into a body of firm, compact substance in which a not well defined, concentric lamination is visible. A microscopic examination of the powdery material from the centre, when mixed with distilled water, shows it to be a mass of bacilliform crystals in ill-defined spheroidal masses, of which the component elements evince no proper disposition; even the projecting peripheral crystals of such masses project without order, in all directions. Here and there a spherule is to be encountered in which the bacilliform elements are radially disposed. The addition of hydrochloric acid brings about a solution of the clusters, the disappearance of which is accompanied by their local replacement with coarse crystals of uric acid. Of a portion of the compact body of this calculus I prepared a microscopic section. It is constructed almost solely of a close mass or felt of bacilliform crystals, intermingled with which there are varying numbers of spherules. The spherules are composed of similar minute crystals, but some are mere balls or spheroidal aggregates of such, of which the rod-like elements at the surface project more or less in the radial direction; in other spherules the radial disposition is more regular, but in none is the margin sharply defined as it is in the case of those of ammonium urate, even when the latter bristles with secondary processes (hedgehog spherules). The shortness and fineness of the crystals, again, offer a striking contrast to those which compose the spherules of calcium urate.

As in the case of calculi of ammonium urate, broad zones occur which may consist solely of the bacilliform crystals without any orderly arrangement, or which may consist chiefly of spherules, or of both combined. A few widely separated and narrow concentric zones occur between these broad belts of spherules and discrete crystals. In these the bacilliform elements are quite obvious, and are set radially to the centre of the calculus. Some such narrow zones consist of only a single row of the rods, and thus correspond in their breadth to the length of the latter. In others a second or a third row of rods succeeds, the



different series being separated by what appear as horizontal lines, but which are, perhaps, only planes of apposition. These narrow compact zones may arise directly upon belts of spheres or upon belts of aggregated bacilliform crystals—i.e., they arise without an origin in laterally coalescing spherules. A certain number of the spheres present a well-differentiated centre and periphery—i.e., a single concentric stria. Lateral coalescence may occur for short stretches between such. Judging from their microscopic structure these particular spherules consist of ammonium urate. This may be taken to be the case, as Mr. Le Sueur was able to demonstrate the presence of a small amount of ammonium in the body of the calculus.

The third calculus, P 8, the largest of the three, is Hunterian, and although placed originally amongst human urinary concretions, it is probably from the same source as the other two—viz., a reptilian urinary bladder. Chemically it consists of: Uric acid, 78·36 per cent.; potassium, 13·19 per cent.; ammonium, 3·09 per cent.; calcium, 1·49 per cent.; magnesium, 0·29 per cent.; calcium phosphate, 0·02 per cent.; animal matter, 1·80 per cent.; water, 0·43 per cent.; and traces of sodium sulphate and sodium chloride. The macroscopic section has a compact body precisely like that of P 7, and a less organized, more friable centre.

#### Summary and Remarks.

*Nucleus.*—A survey of the calculi described shows that the nucleus consists, in every instance, of a conglomerate of spherules. These present no indication of arrangement, and appear to be fortuitous aggregates, the elements of which are, probably, held together by the vesical mucus. Finely crystalline, bacilliform, or amorphous urate never *per se* constitutes a nucleus. The only exception (and this not an absolute one) is furnished by the calculus of urate of potassium from the cloaca of an iguana (p. 7, Royal College of Surgeons.) The nucleus of the main calculus is in some cases compound or composite; it may consist, that is, of two or more microscopic calculi surrounded and combined by succeeding deposit. In calculi of calcium oxalate a similar occurrence may be met with. In the communication by Dr. W. M. Ord and myself (*loc. cit.*) an oxalate calculus with a twin microscopic nucleus is included in the series of photomicrographs illustrating the paper. In the case of uratic calculi it is not that the nucleus, strictly speaking, is doubled or multiple, but that the centre is

constituted by two microscopic calculi, each of which consists centrally of an aggregate of spherules succeeded by lamelliform deposit, the calculi becoming subsequently included in a later deposition common to both. The inclusion of similar microscopic calculi in the growing surface is a further occurrence of an allied kind, which is shown in certain of the urate series.

*The Body.*—Upon such an aggregate there proceeds a regular *growth* of further spherules, as distinguished from the deposition and adhesion of such as are independently formed in the urine. That these “grow” upon the surface is evidenced by the fact that they are hemispheres or lesser sectors only—i.e., the centre of the sphere is located on what was at the time the exterior of the calculus, its subsequent growth taking place only on the distal side; the varying proximity of these centres determines the size of the sectors which are produced in connexion with them. From the coalescence of the laterally apposed sectors a continuous zonular lamina results. The sectors, like the complete spheres, are doubly striated; they are resolvable into fine radiating bacilliform crystals interrupted in the concentric direction by structureless lines. The further growth of such a zone may proceed for a considerable distance, but it continues to exhibit a repetition of the double striation, although the lines indicating the lateral apposition and coalescence of the primary hemispheres may cease to be traceable. In addition to this method, a continuous, laminar formation of the doubly striated material may arise *ab initio*, apart from the formation of hemispheres or cones. The bacilliform crystals instead of radiating from separate centres on the growing surface, are regularly set in a direction radial to the centre of the calculus as a whole. The general uniformity of structure is invariably interrupted by the zonular deposition of irregular aggregates of spheres like those which compose the nucleus. In other cases the general uniformity is varied by the deposition of bacilliform crystals, devoid of order, and in this respect differing from the radially disposed series which construct the proper laminae. This material, finally, may be mingled with aggregates of the spherules. As these atypical depositions are not of uniform thickness, but are irregularly heaped up, the succeeding laminae are thrown into corresponding undulations. These details explain the granularity which the exterior of uratic calculi may present. The cross-striation which is produced by the intervention of what appear as clear lines, is possibly the result of periodic, automatic desaturation of the urine, whereby temporary cessations in the crystalline growth are brought about. This

subject I have more fully referred to in my previous paper on the structure of uric acid calculi.<sup>1</sup> Whatever explanation holds for the cross-striation of the general laminae holds, also, for the concentric striation of discrete spheres. And it may be noticed that in the smaller spheres this is absent, as though the sphere had started into existence in a supersaturated urine, and from juxtaposition with its neighbours had then ceased to grow. Some of the spheres may be compound, or exhibit a lobulated centre of radially set crystals succeeded by a clear encircling line, upon which the radial construction reappears.

#### A Comparison of the Elements occurring in Uratic Calculi, with Urinary Sediments of Urate.

The various elements occurring in these calculi may all be matched in urinary sediments of urate. Of the amorphous granular urate I have encountered none, or little, in the calculi. Urate in this finely divided form is, one may suppose, incapable of cohering so as to produce an aggregate which might form a nucleus.

The urate in calculi occurs essentially in the form of fine crystals which I have ventured to name, from their minuteness and rod-like character, bacilliform. These crystals may be radially disposed in compact spheres or set radially upon the growing surface of the calculus. The smaller spheres exhibit only a radial striation; in the case of the larger, a concentric striation affecting the periphery or crust is super-added. The concentric markings may be explained as due to periodic interruptions in growth arising from local desaturation of the urine.

These varieties of spherular form are encountered also in urinary sediments. In sedimentary spheres of smaller size there is a fine radial—i.e., crystalline—striation, and nothing more. But in those of large size, which are uncommon and not figured even in the Atlas of Rieder and Delépine,<sup>2</sup> or that of Daiber,<sup>3</sup> there is a sharply defined, radially striated, nucleus, succeeded by a crust of varying thickness, in which the radial striation may be equally clear, though it is markedly more delicate.

In the sediments, as in the calculi, moreover, dumb-bells and conoidal groups of fine bacilliform crystals are to be met with (pl. vii, figs. 3 and 5, Rieder and Delépine, loc. cit.). In some cases there occur in the spherular aggregate constituting the nucleus of a calculus, well-

<sup>1</sup> *Proceedings*, 1911, iv, p. 141.

<sup>2</sup> Rieder and Delépine, "Atlas of Urinary Sediments," 1899.

<sup>3</sup> Daiber, "Mikroskopie der Harnsedimente," 2nd ed., 1905.

defined spheres which are beset with a certain number of spines so distinctive of the "hedgehog" forms of acid ammonium urate.

The spheres of calcium urate in the calculi correspond with those sometimes encountered in urinary sediments, and are of large size, constructed of comparatively coarse crystals, and having a deeply frayed edge, from the projection of their free ends. A single sedimentary sphere of calcium urate, from the urine of a gouty patient, is figured in the atlas of Rieder and Delépine (fig. 6, p. 37).

Interposed between the regularly constructed zones of the body of urate calculi there occur others which consist of fine rod-like, or bacilli-form crystals, deposited without any order, and sometimes intermingled with spheres. Crystals of this kind, in a discrete form, are but rarely encountered as uratic sediment.



One of a collection of unusually large sedimentary urate spheres, showing a striated nucleus and a more finely striated crust, indicative of its radially crystalline structure.  $\frac{1}{2}$  oil immersion. (For this sample of urine I am indebted to Dr. Dudgeon.)

Rieder and Delépine (loc. cit., pl. xxii, fig. 2) figure such (of acid ammonium urate), both isolated and in irregular stars, from urine which had undergone ammoniacal fermentation; and Daiber (loc. cit., p. 8), remarks of sodium and potassium urates that they are mostly amorphous but may be finely crystalline, the crystals being arranged in sheaves. He figures none, however, in the discrete or isolated form.

The urate, in whatever form of aggregation it occurs in calculi, is invariably of a pale yellow tint, and in this presents a marked contrast with calcium oxalate, which, even in its finest crystalline forms in calculi, is perfectly colourless. This difference is particularly appreciable when an oxalate zone is intercalated amidst the urate.

The microscopic sections of urate calculi, however thinly ground, lack the beautiful transparency of those of calcium oxalate or of uric acid, and are, in consequence, less well adapted for photomicrography. This arises from the minute state of crystalline subdivision which the uratic formation invariably presents.

### The Organic Matrix in Calculi.

It has long been known that calculi of uric acid, and those of calcium oxalate, contain an organic matrix, which is readily demonstrable by treating minute fragments beneath the microscope—of the first with caustic potash solution, and of the second with hydrochloric acid. Under such circumstances the form and size of the fragment are exactly maintained and represented by a transparent, structureless matrix, which in the case of calcium oxalate exhibits even the radially crystalline structure of the original. This matrix I have demonstrated even in a prehistoric Egyptian calculus of uric acid, the age of which was at least 7,000 years.<sup>1</sup> In the case of urate, if a minute fragment of a typically laminated ammonium urate calculus is examined in distilled water, and hydrochloric acid run beneath the cover-glass, a beautifully transparent matrix is disclosed, which retains the form and size of the fragment, and exhibits quite clearly the fine concentric laminæ of the original. The solution of the urate is accompanied with the appearance of uric acid crystals in the neighbourhood, and on the edges, of the fragment.

I have been able to demonstrate the presence of a similar matrix in an appendicular calculus. Fragments of this, which exhibited the radial striation and concentric lamination common to concretions in general, were readily dissolved in hydrochloric acid, a nebulous matrix being left; a small amount of gas was evolved, the inorganic salts consisting mainly of phosphate and carbonate of lime. A study of the intestinal calculi which are comparatively common in the horse, conducted by the same method, discloses a similar matrix, which exactly retains the form of the coarse radial crystalline columns constructing the concretion.

This being true of concretions in general, the question naturally arises whether it must not hold equally of the individual crystals which compose urinary sediments. In the case of uric acid sediment, I independently discovered the presence of the organic matrix in 1904, though the same observation had been made by Moritz in 1896, and, is recorded in the Transactions of the Fourteenth Medical Congress, held in Wiesbaden, p. 323.<sup>2</sup> A careful examination of the common sedimentary octahedra of calcium oxalate whilst treated beneath the microscope with hydrochloric acid will, I find, reveal the presence of

<sup>1</sup> *Trans. Path. Soc. Lond.*, 1905, lvi, p. 275.

<sup>2</sup> *Verhandl. des Congr. f. inn. Med.*, Wiesb., 1896, xiv, p. 323.

the same substance. And the same thing holds of sedimentary spherules of urate when submitted to the action of the same acid.

To give a detailed account of one of a series of observations made by myself in 1904, upon uric acid sediment from four different cases: Urine—specific gravity, 1023; acid; no sugar; no albumin; amorphous urate, and uric acid (cayenne pepper) deposit. The uric acid sediment was washed in distilled water; the crystals were discrete and of the ordinary rhomboidal form. Treated under the microscope with caustic potash solution, the clear, pale yellow substance slowly disappeared, the form of the crystal being exactly retained and represented by a transparent uncoloured matrix. The process of solution can be witnessed as it occurs from without inwards, the central part persisting longest. The clear matrix so disclosed grows afterwards less transparent, and becomes strewn with fine darker points. On running distilled water under the cover-glass, the dark granular appearance vanishes; this suggests that the granularity results from the secondary production of potassium urate in the matrix. Spherules and dumbbells of the last-named salt appear between the crystals or cling to the exterior of the deuricized matrix.

I may append a figure of the matrix of a group of uric acid crystals after treatment with caustic potash solution. The microscopic preparation was made in October, 1904, and has since then been preserved in dilute glycerine; the matrix is slightly creased or folded from contraction, otherwise it retains the proper form of the crystals composing one of the clusters which the urine contained. The deposit had never been allowed to dry; it was kept in distilled water for a week in a test-tube, and frequently washed. Such crystals as exhibit striæ due to secondary cleavage, or other internal structure, continue to do the same after being deuricized (*see* pl. ii, fig. 12).

In regard to the nature of this matrix, it cannot be supposed that it is some hitherto unrecognized proteid, a urinary argon, the presence of which is revealed only by the process of crystallization. It consists wholly or in part of mucin. That it may consist solely of this substance is proved by the fact that the urate of ammonium spherules which may form in normal urine during ammoniacal fermentation, exhibit the same matrix. Thus in a sample of normal urine (*sanguinis*) allowed to undergo ammoniacal fermentation in a flask plugged with cotton-wool, along with amorphous calcium phosphate and feathers of ammonio-magnesium phosphate, there was a nut-brown sediment of spherules of ammonium urate. The spherules were washed



in distilled water, and first examined in this; they were sharply defined, without concentric striæ, and exhibited quite clearly the fine radial striation indicative of their crystalline structure. Under the action of hydrochloric acid a very delicate, transparent matrix was disclosed as the urate was dissolved; in this the fine striation even of the original urate was clearly retained.

When albumin is reaching the urine from an inflamed vesical mucosa, or through the kidney, this will take part in the formation of the matrix. This question may be approached synthetically by studying crystals artificially produced in a solution of blood albumin. As it is immaterial what crystals are studied, I selected potassium nitrate, at Mr. Le Sueur's suggestion, since the crystals of this salt are particularly coarse, and rapidly producible. A strong solution of Merck's pure blood albumin was made in distilled water, and this, after filtration, was saturated with potassium nitrate. The saturated solution was again filtered, and a few drops allowed to dry at 37° C. on the centre of a series of slides.

A dense, white, opaque film results, in which the long, coarse crystals of the salt are easily visible even to the naked eye. The film being under observation beneath  $\frac{1}{4}$  objective, and without a cover-glass, formol solution (40 per cent.) was allowed to act from its edge. This readily dissolves the potassium nitrate, without dissolving the albumin. Under these circumstances, as the crystals undergo solution, a distinct albuminous matrix is brought into view in their place; the matrix of the crystals appears closer in texture and has a different grain from that of the albumin in which they are embedded.

The observation may be modified by heating the film after it is dried, so as to completely fix the albumin; the use of formol solution will, as before, reveal the albuminous matrix of the crystals as the potassium nitrate is dissolved.



## **Thyroid Action and Reaction, with Special Reference to the Formation of Thyroid Tumours.**

By RUPERT FARRANT.

FOUR main ductless glands are developed from the primitive pharynx: the tonsil, the anterior lobe of the pituitary, the thymus, and the thyroid. Of these, the thymus and tonsil are lymphoid in character, and one of their functions is the formation of lymphocytes, and though the exact functions of lymphocytes is at present unknown, I think we may for the purpose of analogy look on them as being concerned in the first line of defence against certain micro-organisms. The anterior lobe of the pituitary and the thyroid are secretory glands. Can either one or both of these act as the second line of defence for the destruction of some poisons that some micro-organisms produce?

The thyroid, as opposed to the thymus, continues to grow and obtains a very free blood supply. The gland secretion reaches the circulation by means of the veins. It was thought at one time that the secretion was absorbed by means of the lymphatics; this has been shown to be erroneous. Carlson and Woelfel [1] collected the lymph coming from the thyroid in dogs and found it to be inactive and to contain no iodine. The substance taken for colloid entering the lymphatics has since been shown to be indistinguishable from coagulated lymph [3].

### **THE ANATOMY OF THE THYROID VEINS.**

There are six thyroid veins; of these four open on the left side and two on the right, owing to the inferior thyroid veins opening either singly or together into the left innominate vein. The inferior thyroid veins are the largest, thus more than two-thirds of the thyroid secretion reaches the left side by means of the thyroid veins. Is there any reason for this? The left innominate vein receives the thoracic duct, the right innominate vein the right lymphatic trunk. The thoracic duct drains more than two-thirds of the total lymph area, and the right lymphatic trunk less than one-third. Thus the thyroid veins and the lymphatic trunks correspond in size. The thyroid veins may be said to guard the openings of the terminal lymphatic trunks. The right upper and middle thyroid veins open into the right internal jugular above the

opening of the lymphatic trunk, the left upper and middle thyroid veins open into the left internal jugular above the thoracic duct, and the two inferior thyroid veins into the left innominate below it.

Variations occur in both the thyroid veins and in the thoracic duct, but I have been unable to discover whether in their various anomalies these anatomical relations and proportions are true. The thoracic duct normally carries lymph and chyle, but we know that certain toxins are absorbed by the lymphatics and reach the circulation via the thoracic duct and right lymphatic trunk. The chyle and certain toxins thus enter the circulation at a place where there is a maximum quantity of thyroid secretion in the blood, and before reaching the central nervous system and tissues generally they will be exposed to the action of iodine in organic combination and oxygenation in the lungs.

We know that the thyroid has a marked influence on the metabolism of fat. Has it also any influence in the destruction of toxins? If so, one would expect a reaction and evidence of increased secretion in certain toxæmias. To-night I only propose to show the reaction that the thyroid undergoes in some of the simplest toxæmias, where, as far as possible, any previous change can be eliminated.

#### OBSERVATIONS ON THE THYROID IN CLINICAL TOXÆMIAS.

The following are the changes that occur: Firstly, the colloid becomes finely granular; secondly, it becomes vacuolated and partially absorbed; thirdly, an alternation occurs in the cells, they become more numerous, elongated, approaching the columnar type and arranged in masses; fourthly, the colloid becomes entirely absorbed and the walls of the vesicles become crenated and infolded; fifthly, the infolding and cell increase go on to transform the vesicles into solid masses of cells. These changes go on side by side so that several of them may be seen in the same section, but the section is placed according to the change that is most marked.

*The First Series is one of Infantile Diarrhœa.*—Simpson [10] noted colloid absorption and cell infiltration in marasmus and acute diseases. Section 1 (see p. 34) shows slight granulation and absorption of the colloid, otherwise it is normal. Section 2 shows a further absorption of colloid, and the cells are beginning to alter in shape. Section 3 shows an increased cell reaction and how the colloid is being eaten away at its edges. Section 4 shows the colloid entirely absorbed, and

the vesicles are transformed into solid masses of cells by the infolding of their walls. Section 5 shows half of the first and last of this series under the low power, the left side showing the colloidal thyroid, and the right the hyperplastic thyroid: they were both taken from uncomplicated cases of infantile diarrhœa, the only difference being the duration of the disease; but, as in infantile diarrhœa, one has to depend on the history, the exact duration cannot be obtained, but the series is roughly arranged in the order of the disease from early to late stages.

*Second Series: From Cases of Diphtheria.*—Section 6 (see p. 36) shows the granulation and absorption of the colloid; this was a case of hæmorrhagic diphtheria of four days' duration. Section 7 shows the granulation of the colloid very well and early cell reaction. This patient died on the seventh day of the disease. Section 8 shows total colloid absorption, the elongated type of cell and crenation and infolding of the lining wall for the formation of cell masses. This patient died on the seventh day and was of a very severe type. Section 9 shows marked cell reaction; the cells are columnar in type, the infolding of the walls of the vesicles having produced solidification. This patient died on the twelfth day. Section 10 shows half of the first of the first and last of this series to compare the extent to which this reaction has gone on during eight days; on the left is the thyroid hyperplasia of late diphtheria, on the right the almost normal thyroid of early diphtheria. The patient with the latter died on the fourth day, that with the former died on the twelfth day.

*Third Series: From Cases of Measles and Broncho-pneumonia.*—Section 11 (see p. 39) shows that the colloid is entirely absorbed and the walls of the vesicle are commencing to fold inwards. This patient died on the tenth day. Section 12 shows total colloid absorption, with infolding of the vesicles. This patient died on the fourteenth day. Section 13 shows complete thyroid hyperplasia, with solidification of the vesicles. This patient died on the eleventh day. Section 14 shows the comparison under the low power of two of these sections—a difference of even one day can be detected by the thyroid change. The right side is taken from a patient who died on the ninth day, the left from one who died on the tenth day. However, as it is, of course, impossible to say when the pneumonia started, the dates of this series cannot be entirely accurate.

*Fourth Series: From Cases of Whooping-cough and Broncho-pneumonia.*—Section 15 (see p. 41), under the low power, shows the

granulation and absorption of the colloid. This patient died on the fourth day. Section 16, under the high power, shows a much further stage—total colloid absorption with the walls of the vesicles infolded; the cells are apparently being directly changed into colloid. This patient died on the fifteenth day. Section 17, under the low power, shows very well the infolding of the walls of the vesicles by which they become solidified. This patient died on the thirty-seventh day. These plates are somewhat small, so the slides themselves are also shown in series under the microscope. These changes occur so regularly and exactly that in any given group it is quite an easy matter to arrange them in the order of the duration of the disease. What is the significance of this reaction? Is it simply a reaction for increased metabolism or is it a reaction for the production of antitoxin? One can dismiss at once the idea of its being simply a reaction for increased metabolism, as the thyroid only reacts in the way I have described to certain diseases; other diseases, such as infections with streptococcus, staphylococcus, or *Bacillus coli communis*, even if accompanied by high fever, do not produce this reaction. I am afraid that time does not allow me to arrange these toxæmias into groups according to the organisms that produce them.

I propose now to try and prove that this reaction is antitoxic in function.

#### EXPERIMENTAL TOXÆMIA.

If thyroid reaction is produced by the effect of the toxins, the same changes should occur in guinea-pigs when injected with diphtheria toxin. A number of guinea-pigs were daily given diphtheria toxin in doses from the minimal lethal to one-eighth part of it.

*First Series.*—Section 18 (see p. 42) shows the thyroid of a normal guinea-pig; (five sections were shown of the thyroids of guinea-pigs dead on the second, third, fourth, fifth, and sixth days respectively of diphtheria toxin; the changes were similar to those shown previously from early diphtheria in children, colloid absorption, and cell reaction). Section 19 shows this typical cell reaction and colloid absorption; this guinea-pig died on the fifth day after injection. Thus diphtheria toxin can produce the reaction. Half of these guinea-pigs were at the same time given thyroid powder by the mouth in doses from 0.05 gm. to 0.01 gm. The doses of the toxin and the thyroid powder were continued daily until they died. The animals to which thyroid was given

were exactly similar in appearance and weight to those to which the toxin was given alone.

*Second Series.*—This showed the same changes, but less marked. The five guinea-pigs died on the second, third, fourth, fifth, and sixth days respectively, and were given thyroid by the mouth as well as daily injections of toxin. Section 20 shows the terminal thyroid hyperplasia of a guinea-pig dead on the seventh day after injection. The reaction in the series was distinctly less in those guinea-pigs that were given thyroid as well as toxin.

#### HAS THYROID FEEDING ANY ANTITOXIC ACTION TO DIPHTHERIA TOXIN?

A further series of fourteen guinea-pigs was arranged in seven pairs and were injected with different doses of toxin. Half were otherwise untreated, while the other half were given thyroid powder every day; the dose of thyroid varied with the dose of toxin.

TABLE I.

| Weight | Toxin, daily dose | Thyroid daily | Days of toxin | Days of thyroid | Died, days | Weight loss |
|--------|-------------------|---------------|---------------|-----------------|------------|-------------|
| 220    | 0.6               | —             | 4             | —               | 5          | 50          |
| 215    | 0.6               | 0.04          | 4             | 4               | 6          | 70          |
| 200    | 0.5               | —             | 4             | —               | 5          | 45          |
| 205    | 0.5               | 0.03          | 4             | 4               | 5          | 50          |
| 165    | 0.4               | —             | 4             | —               | 5          | 45          |
| 160    | 0.4               | 0.03          | 4             | 4               | 7          | 45          |
| 270    | 0.5               | —             | 2             | —               | 2          | —           |
| 260    | 0.5               | 0.05          | 2             | 3               | 2          | —           |
| 190    | 0.2               | —             | 3             | —               | 3          | 30          |
| 190    | 0.2               | 0.04          | 3             | 4               | 3          | 45          |
| 180    | 0.15              | —             | 2             | —               | 2          | —           |
| 180    | 0.15              | 0.03          | 3             | 5               | 4          | 30          |
| 180    | 0.05              | —             | 2             | —               | 2          | —           |
| 190    | 0.05              | 0.01          | 3             | 5               | 4          | 55          |

The minimal lethal dose of the toxin used was 1 c.c. when given in one injection.

It can be seen from the table that, of the seven pairs, four of those given thyroid outlived those not given thyroid; the other three pairs

died on the same day. These guinea-pigs were injected every day, as I wanted their thyroids to confirm the changes shown in the last series of slides; these changes were confirmed. To a certain extent the giving of thyroid resisted the action of the diphtheria toxin, but the daily pricking with the needle discounts almost entirely any antitoxic effect, as guinea-pigs die if repeatedly pricked with a needle.

A further series of twelve guinea-pigs were given a single injection of one and a half times the minimal lethal dose of diphtheria toxin. Half of them were given 0.3 gm. of thyroid in three doses of 0.1 gm. during the forty-eight hours previous to injection. All the guinea-pigs previously given thyroid powder outlived the other guinea-pigs (*vide* table).

TABLE II.

| Weight |     | Died in days |     | Thyroid, grammes of |
|--------|-----|--------------|-----|---------------------|
| 270    | ... | 5            | ... | —                   |
| 270    | ... | 7            | ... | 0.3                 |
| 320    | ... | 2            | ... | —                   |
| 325    | ... | 3            | ... | 0.3                 |
| 210    | ... | 1            | ... | —                   |
| 220    | ... | 2            | ... | 0.3                 |
| 265    | ... | 4            | ... | —                   |
| 265    | ... | 5            | ... | 0.3                 |
| 275    | ... | 3            | ... | —                   |
| 255    | ... | 5            | ... | 0.3                 |
| 290    | ... | 5            | ... | —                   |
| 315    | ... | 6            | ... | 0.3                 |

One can say from this series that those guinea-pigs previously fed on thyroid resisted the effect of one and a half times the minimal dose of toxin longer than those not so fed.

#### IS THE SERUM OF A THYROID-FED ANIMAL ANTITOXIC?

Two rabbits were fed with 0.5 gm. of thyroid daily by the mouth until one died, on the seventh day, of hyperthyroidism. The other was bled and its serum collected. Ten guinea-pigs were arranged in pairs; this serum was used on five of them in doses from 0.9 c.c. to 0.25 c.c. to protect them from one and a half times the minimal lethal dose of toxin.

TABLE III.

| Weight                       | Toxin,<br>cubic centimetres of |     |     | Serum |     | Died, days |     | Lived |
|------------------------------|--------------------------------|-----|-----|-------|-----|------------|-----|-------|
| 280                          | ...                            | 1.5 | ... | —     | ... | 6          | ..  | —     |
| 270                          | ...                            | 1.5 | ... | 0.9   | ... | —          | ... | Yes   |
| 270                          | ...                            | 1.5 | ... | —     | ... | 2          | ... | —     |
| 250                          | ...                            | 1.5 | ... | 0.6   | ... | —          | ... | Yes   |
| 290                          | ...                            | 1.5 | ... | —     | ... | 4          | ... | —     |
| 280                          | ...                            | 1.5 | ... | 0.5   | ... | 4          | ... | —     |
| (Died of an abscess in neck) |                                |     |     |       |     |            |     |       |
| 235                          | ...                            | 1.5 | ... | —     | ... | 3          | ... | —     |
| 240                          | ...                            | 1.5 | ... | 0.3   | ... | —          | ... | Yes   |
| 270                          | ...                            | 1.5 | ... | —     | ... | 4          | ... | —     |
| 270                          | ...                            | 1.5 | ... | 0.25  | ... | —          | ... | Yes   |

So all those guinea-pigs given the serum of a thyroid-fed rabbit lived except one, which died from an abscess which developed in its neck. This shows that the serum of thyroid-fed animals is antitoxic to diphtheria toxin.

#### DOES DIPHTHERIA ANTITOXIN CONTAIN MORE THYROID SECRETION THAN NORMAL SERUM?

A rabbit was fed on not less than 4,000 units of diphtheria antitoxin a day, about 10 c.c. in amount. The antitoxin was mixed with its food. This rabbit developed exactly the same symptoms as those produced by thyroid feeding—loss of weight, tachycardia, fur changes, &c. It died at the end of sixteen days, having lost 31 per cent. of its weight; it dropped from 1,690 gm. to 1,160 gm. The post-mortem changes were similar to those of a rabbit dead from thyroid feeding—absence of fat, wasting of the muscles, dilatation of the heart, &c. Another rabbit weighing 1,170 gm. was fed on 10 c.c. normal horse serum a day. This rabbit exhibited no signs of thyroid excess, and instead of losing weight it put on 85 gm. in sixteen days.

If diphtheria antitoxin contains an excess of thyroid secretion it should have no ill-effect on thyroidectomized animals. A young rabbit weighing 905 gm. was thyroidectomized. At the end of ten days its wound was healed and it had regained to within 15 gm. of its former weight. It was given not less than 2,000 units of diphtheria antitoxin a day, that is, the units given per body-weight were roughly proportional to those of the former experiment. At the end of fourteen days it had



put on 250 gm. in weight and showed no ill-effects from the feeding. At the end of seven weeks it weighed 1,220 gm. So diphtheria antitoxin is harmless when fed to thyroidectomized rabbits, but normal rabbits when fed with it develop symptoms of thyroid excess and die.

#### OBSERVATIONS ON ANTITOXIN.

We should be able to gain some confirmation of thyroid reaction and its relation to diphtheria antitoxin by the examination of the thyroids of horses that have been used in the preparation of antitoxin. These horses are injected with increasing doses for about a year, with periods of bleeding and periods of rest. A week to ten days from the last injection of toxin the horses are finally bled out, as after several bleedings the antitoxic value of the serum falls so that it is of no practical use.

*Horse Series.*—Section 21 (see p. 44) shows an active hyperplasia with small vesicles containing some colloid, the feature of the section being the masses of cells in the centre of which colloid is being formed. Section 22 shows an active hyperplasia with colloid in larger vesicles; the active formation of the colloid is well seen by the rows of cells gradually shading off into colloid material. This method of the production of the secretion is similar to that occurring in sebaceous glands [2]. Section 23 shows a further formation of colloid, the cells being squeezed together between the enlarging vesicles. Section 24 shows a more advanced stage of colloid formation, though the hyperplasia can still be seen by the number and active type of the cells. Section 25 shows the comparison under the low power of the first and last of this series, the one on the left the hyperplasia, the one on the right the colloid formation.

This series of horse thyroids is arranged in order of hyperplasia, the first being most marked, the last least. The antitoxic value runs in the reverse order; the serum of the first horse was only valued at 200, whilst the last was 300.

Is there any relation between thyroid hyperplasia, its iodine value, and the antitoxic value of the serum? Marine and Williams [7] estimated the amount of iodine contained in various conditions of thyroids and found that it was less in hyperplasia than in normal or in colloid glands. Marine and Lenhart [4] showed by numerous experiments that the hyperplasias always in time revert to colloid glands, and that this change was hastened by the administration of substances containing iodine. In these observations on the horse hyperplasia of the thyroid

was accompanied by a low antitoxic value of the serum, but I have had no opportunity of estimating the amount of iodine contained in these glands. But if hyperplasia varies inversely with the iodine content, as Marine and Williams [7] state, the glands of the horses associated with low antitoxic value would show a low iodine value.

I have had, and still am having, the iodine content estimated in the various sera. This work has been carefully done for me by Mr. Bosworth at the Westminster Hospital Medical School Laboratories, according to Oswald's [9] modification of Baumann's method.

The following are the results for anti-diphtheritic serum :—

One gramme of dried serum contained 0.036 mgrm. of iodine in organic combination.

|   |   |   |        |   |   |   |
|---|---|---|--------|---|---|---|
| " | " | " | 0.031  | " | " | " |
| " | " | " | 0.0259 | " | " | " |

The last of these was of too low an antitoxic value to be used for injections.

The estimation for normal horse serum was that it contained less than 1.6 parts per million of serum. So we find the amount of iodine present in the serum is much larger in the toxin-treated horse than in the normal animal. Marine and Williams [7] also showed that the physiological value of the thyroid varies with its percentage of iodine; and as far as my estimations go they show that the value of the diphtheria antitoxic serum also varies with its iodine content; though I shall before long be able to present you with a larger and more convincing series.

Taking these results together: Certain toxins stimulate the thyroid into a condition of hyperplasia; during this change it seems probable that the iodine-containing substances are poured out into the circulation, for the serum of the immunized horse contains an excess of iodine, while the thyroid is hyperplastic. I assume from the experiments of Marine and Williams that the thyroid itself becomes deficient in iodine at the same time. During the reversion back to the colloid the iodine is once more taken up by the thyroid, and it changes back to the colloid gland; the rate of change is directly proportional to the amount of iodine present.

## SUMMARY.

(1) The thyroid undergoes hyperplasia in certain diseases. This hyperplasia resembles that following partial thyroidectomy. A similar hyperplasia is induced in guinea-pigs by the injection of diphtheria toxin, and is mitigated if thyroid administration be combined with the diphtheria toxin. These guinea-pigs also survive longer than the controls.

(2) The blood serum of a thyroid-fed rabbit is antitoxic to diphtheria toxin.

(3) Antitoxin fed to normal rabbits produces symptoms similar to those arising from feeding thyroid, while in thyroidectomized rabbits antitoxin is borne without symptoms.

(4) Diphtheria antitoxin contains iodine in organic combination; normal horse serum contains but the slightest trace. This indicates some close relationship between the thyroid function and the development of certain antitoxins. It may be suggested that the hyperplasia observed in these toxæmias arises from the attempt to form antitoxin.

## THE FORMATION OF THYROID TUMOURS.

(a) *From the Normal to Hyperplasia.*—The toxins that produce thyroid hyperplasia may be divided into two main groups: the exogenous, where they are supplied from without; and the endogenous, where they are produced within the body. The production of thyroid hyperplasia by exogenous toxins has been shown by Wilms, who produced it in rats by giving them water from an infected well. Marine and Lenhart [5] examined the cause of the hyperplasia in the pike and bass of Lake Erie, the brook trout of the Pennsylvania Fisheries [6], and found the latter due to the polluted water. McCarrison found that water containing coliform organisms produced it in man. It was not all the rats or all the patients, and only 6 per cent. of the fish so exposed, that developed an enlargement of the thyroid. From the slides I have shown one saw that certain endogenous toxæmias produce hyperplasia of the thyroid; most of these involute back again and no thyroid enlargement is produced, though some may go on to definite enlargement. So in both endogenous and exogenous, if the toxins be withdrawn early, the hyperplasia will disappear. McCarrison [8] showed in the exogenous that

even when the hyperplasia has gone to a general enlargement, if the toxæmia be removed, the gland will regain its normal size. As regards this, for the endogenous toxins I can show it better clinically. Section 26 (see p. 46) shows on the left the hyperplasia from a case of exophthalmic goitre, on the right the hyperplasia produced by a case of measles and broncho-pneumonia of eleven days' duration. The two halves are very similar; microscopically the vesicles are a little more broken in the exophthalmic portion, and macroscopically it formed an enlargement of the thyroid, whilst the measles did not. The earliest stage of hyperplasia would not produce an enlargement of the thyroid, but rather a diminution of size from absorption of the colloid material.

(b) *Hyperplasia to Colloid*.—Marine and Williams [7] found that all thyroid hyperplasias in dogs have an increased capacity for iodine and for colloid formation, and from their experiments proved that a thyroid circle takes place from the normal gland to hyperplasia and from hyperplasia to the colloid gland. The reversion from the early hyperplasia due to endogenous toxins to the colloidal type of gland is well seen in section 27. The left portion shows a hyperplasia, due to whooping-cough and broncho-pneumonia, dead on the thirty-seventh day. The right portion is from a similar case, the patient dying three to four months after the recovery from the broncho-pneumonia; the cause of death was a toxæmia that has no effect on the thyroid. Section 28 shows on the left a thyroid from an exophthalmic gland, and on the right a colloidal gland from a later stage of a similar case. Section 29 shows the comparison between the involution of an early hyperplasia on the left and that of a late hyperplasia on the right. During this process of excessive colloid formation the thyroid would increase in size, and the portion that had been in the highest degree of hyperplasia would have a greater deposit of colloid; this would lead to the formation of the so-called adenoma. Adenomata may develop at any stage of the hyperplasia, and so the adenomata may be combined with the early, moderate, or marked hyperplasia. This process of colloid formation is the form which involution takes in the thyroid and the masses of colloid are inactive, as shown by Stoland [11]. During this involution degeneration changes are liable to take place as in any other gland, the breast for example. The degeneration will show itself in the formation of single or multiple cysts. The rest of the gland may be in any of its stages, so leading to the occurrence of cysts in a hyperplastic gland, or the cyst-adenoma. The involution may go on to fibrosis.

To sum up these changes: Hyperplasia without thyroid enlargement; hyperplasia with various degrees of enlargement; adenomata of involution; cysts and cyst-adenomata of degeneration.

#### THE FORMATION OF THYROID TUMOURS IN CRETINS.

The facts known about cretins may briefly be stated to be that their parents have goitres, and usually live in endemic goitre districts, but that if they remove from the district they no longer bear cretins. So the cause of the thyroid changes in the infant is not the thyroid change in the mother, but the cause that produces these thyroid changes. Seventy-five per cent. of cretins have enlarged thyroids at one period or another. Cretinism usually develops between the first and second years. On examination of the literature one finds exactly the same cycle of changes that occurs in adult thyroids, only the active hyperplasia is rarely seen, and though cases of exophthalmic goitre have been recorded in the newly born, the rate of involution and degeneration is complete in two to three years. There are two facts to account for this: (1) The toxin circulating in the blood of the foetus will be relatively large in amount as it will correspond to the toxicity of the mother's blood; (2) from section 30 it will be seen that the thyroid of the normal foetus is already in a condition corresponding to hyperplasia, and, considering the delicate condition of foetal organs, one would expect the involution and degeneration changes to follow rapidly. It is of interest to note that cretins usually die of those diseases that produce a thyroid reaction in normal beings.

Time prevents me from producing to-night the results of my work on the normal stimulus and the production of the symptoms of thyroid excess. The whole of the experimental work was done at the University College Laboratories, and I cannot say how much I am indebted to Professor Cushny for his care and advice.

I am much indebted to Dr. Braxton Hicks, Dr. McConkey, Dr. Rolleston, and Dr. Thompson, for supplying me with the material that I have used to-night; also to Dr. Cartwright Wood for giving me antitoxin to enable me to repeat some of these experiments.

## REFERENCES.

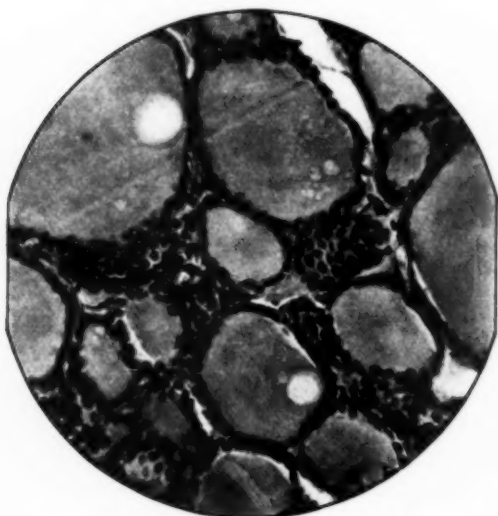
- [1] CARLSON and WOELFEL. *Amer. Journ. of Phys.*, Boston, 1910, xxvi, p. 40.
- [2] *Idem. Ibid.*, p. 63.
- [3] CHAMBERS, H. *Lancet*, 1912, i, p. 680.
- [4] MARINE and LENHART. *Johns Hopkins Hosp. Bull.*, Balt., 1909, xx, pp. 131-39.
- [5] *Idem. Ibid.*, 1910, xxi, p. 95.
- [6] *Idem. Depart. Pennsylv. Fisheries Bull.*, vii.
- [7] MARINE and WILLIAMS. *Arch. Internat. Med.*, Chicago, 1908, i, pp. 349-84.
- [8] McCARRISON. *Med. Chir. Trans.*, 1906, lxxxix, pp. 437-70; *Quart. Journ. Med.*, Oxf., 1908-09, ii, p. 279-88.
- [9] OSWALD. *Zeitschr. f. Physiol. Chem.*, Strasb., 1897, xxiii, p. 265-310.
- [10] SIMPSON. *Scottish Med. and Surg. Journ.*, Edinb. and Lond., 1906, xix, p. 504-19; *Brit. Med. Journ.*, 1910, i, p. 1049.
- [11] STOLAND. *Amer. Journ. Phys.*, 1912, xxx, p. 37.

## ILLUSTRATIONS (pp. 34-48).

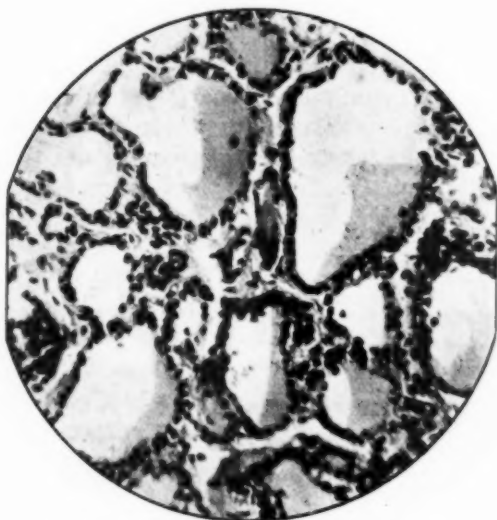
The following illustrations are of some of the slides that were shown. The first four series show the hyperplasia that is produced by infantile diarrhoea, diphtheria, measles, and whooping-cough. The hyperplasia shown in an illustration corresponds to the duration of the disease of its series. The double illustration at the end of each series compares the degree of hyperplasia that has taken place in various periods of time.

The horse series is arranged in order of their hyperplasia, but in the reverse order of the antitoxic value of the serums obtained. The tumour series shows the method of thyroid involution from hyperplasia to colloid formation, including the early hyperplasias that do not, and the late hyperplasias that do, form thyroid tumours.

## SERIES I.—INFANTILE DIARRHŒA.



Section 1.—The first stage of colloid absorption ; granulations at the margins.



Section 2.—Latest stage of colloid absorption.



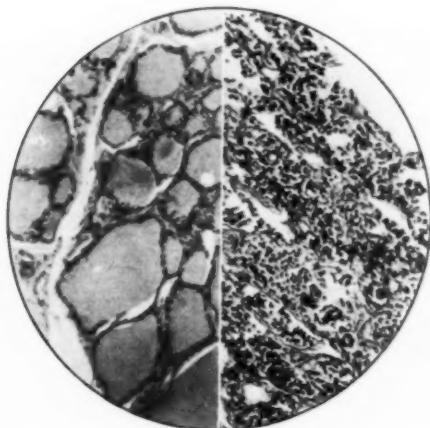
SERIES I.—INFANTILE DIARRHŒA (*continued*).



Section 3.—Colloid eaten away at the edges; cell reaction.

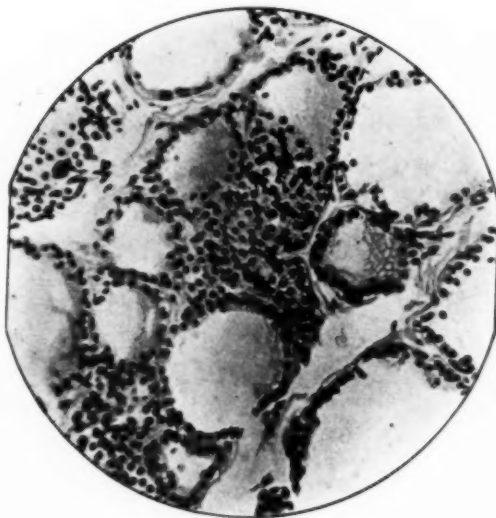


Section 4.—Complete hyperplasia; cellular mass.

SERIES I.—INFANTILE DIARRHOEA (*continued*).

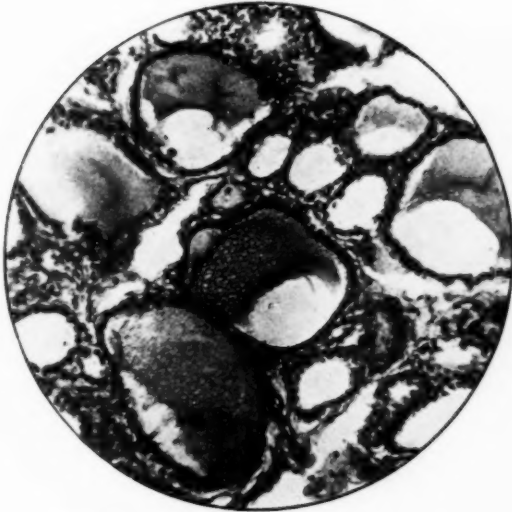
Section 5.—Comparison of early (left) and late (right) thyroid reaction.

## SERIES II.—DIPHTHERIA.

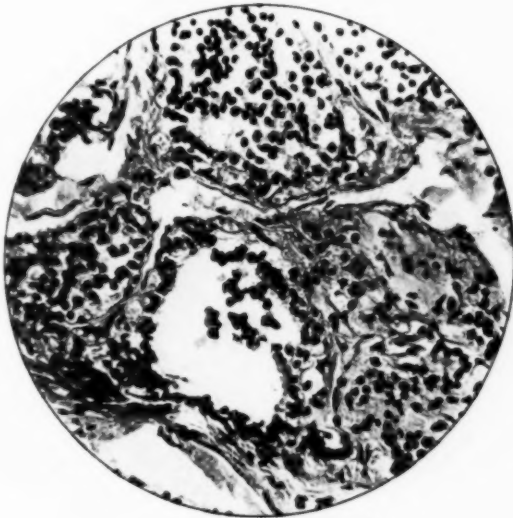


Section 6.—Early thyroid reaction.

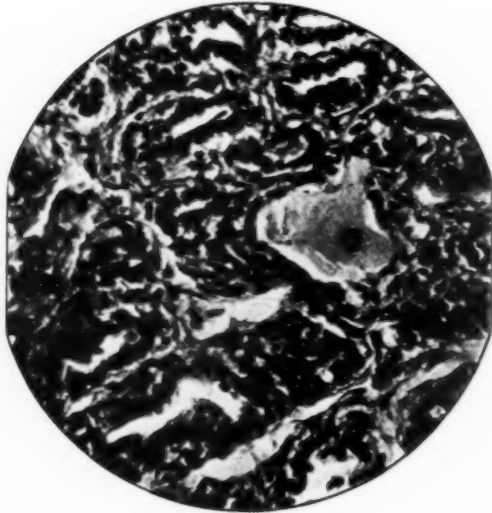
SERIES II.—DIPHThERIA (*continued*).



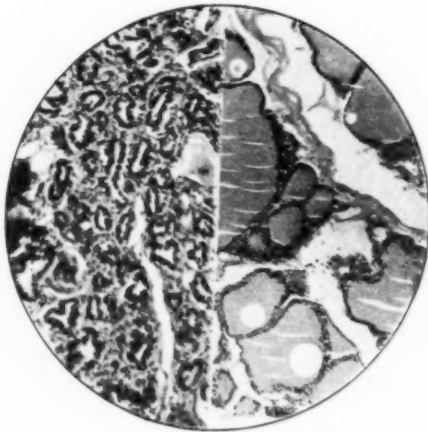
Section 7.—Granulation and colloid absorption.



Section 8.—Medium cell reaction.

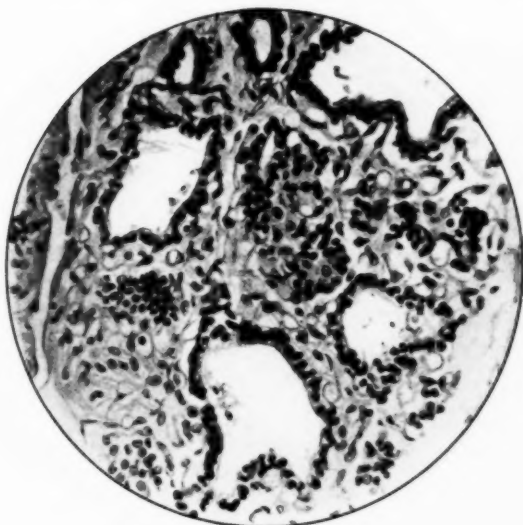
SERIES II.—DIPHTHERIA (*continued*).

Section 9.—Columnar cells; vesicles infolded and crenated. Complete hyperplasia, twelve days.

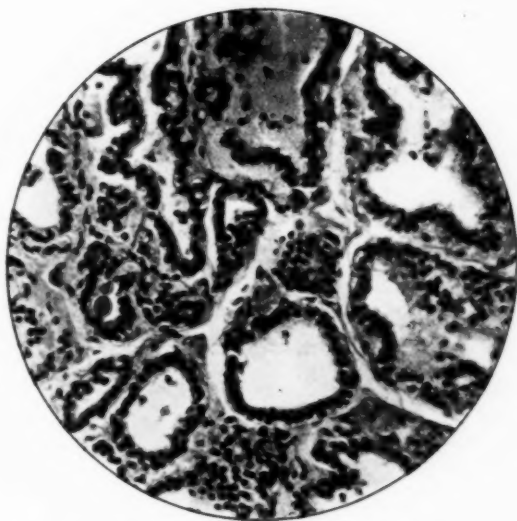


Section 10.—Comparison between twelve days' hyperplasia (left) and four days' hyperplasia (right).

SERIES III.—MEASLES AND BRONCHO-PNEUMONIA.



Section 11.—Colloid absorbed ; commencing crenation.



Section 12.—Colloid absorbed ; vesicles crenated ; cell reaction.

SERIES III.—MEASLES AND BRONCHO-PNEUMONIA (*continued*).

Section 13.—Complete hyperplasia, eleven days.

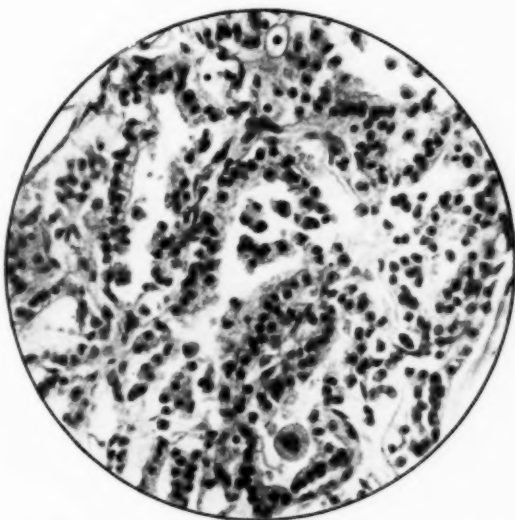


Section 14.—Left side, ten days' hyperplasia ; right side, nine days' hyperplasia.

SERIES IV.—WHOOPING-COUGH AND BRONCHO-PNEUMONIA.

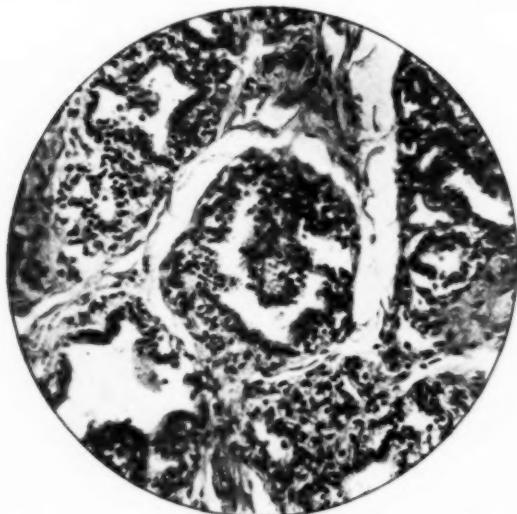


Section 15.—Granulation and absorption of colloid, four days. Low power.



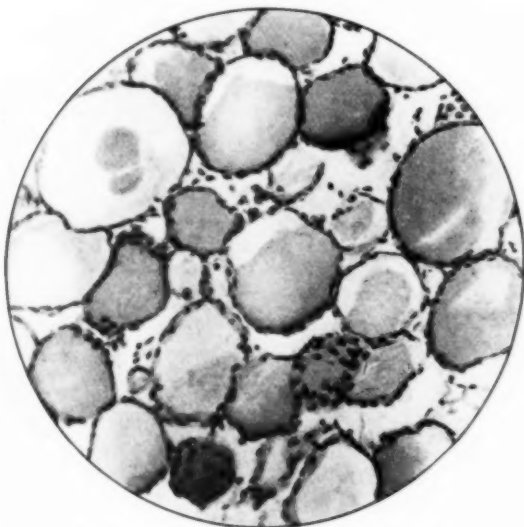
Section 16.—Vesicles infolded, colloid absorbed, fifteen days. High power.



SERIES IV.—WHOOPING-COUGH AND BRONCHO-PNEUMONIA (*continued*).

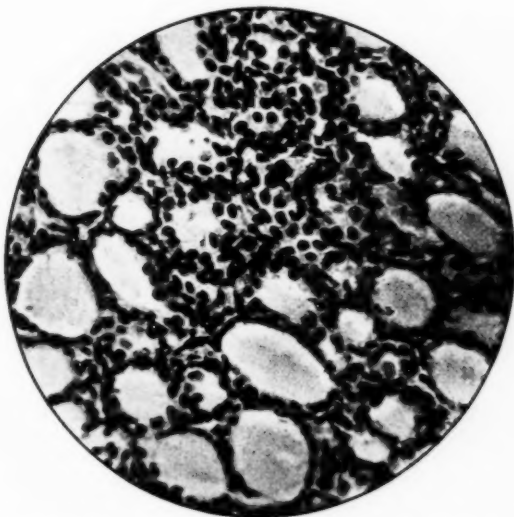
Section 17.—Method of solidification of the vesicles by infolding of their walls.

## EXPERIMENTAL TOXÆMIA.

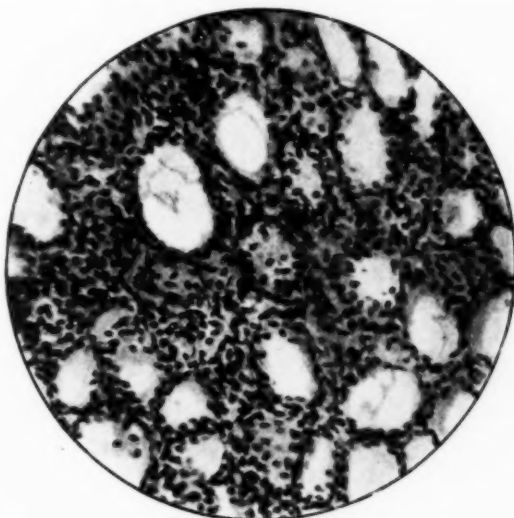


Section 18.—Thyroid from normal guinea-pig.

EXPERIMENTAL TOXEMIA (*continued*).

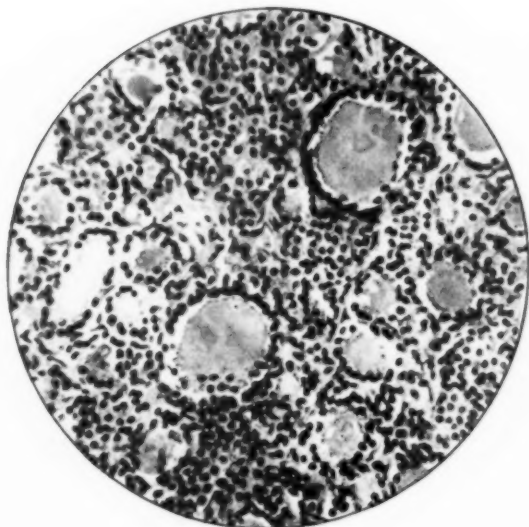


Section 19.—Cell reaction five days after injection with diphtheria toxin.

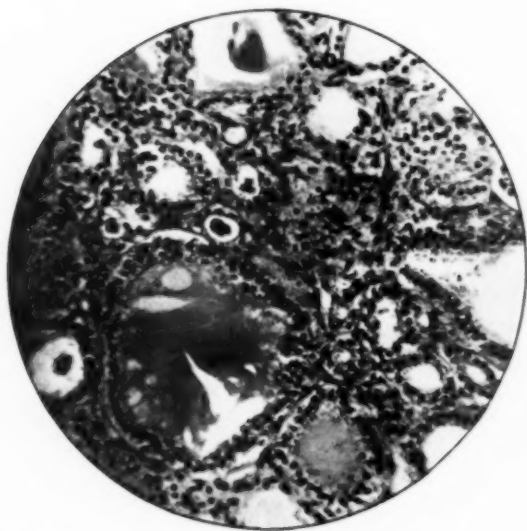


Section 20.—Hyperplasia seven days after injection with diphtheria toxin,  
even with thyroid administration.

## HORSE SERIES.



Section 21.—Active hyperplasia.



Section 22.—Hyperplasia changing to colloid gland by direct transformation of cells into colloid.

HORSE SERIES (*continued*).

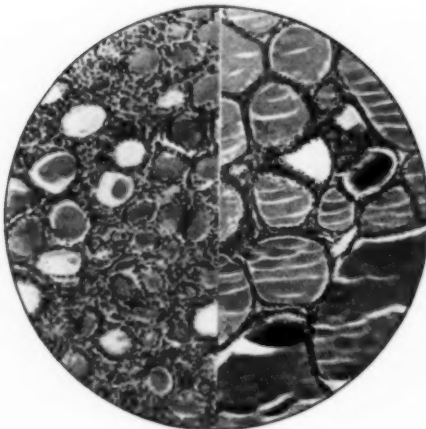


Section 23.—Cells being squeezed into rows by the increasing colloid.



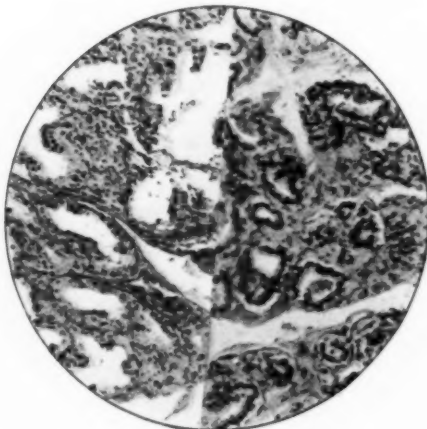
Section 24.—Similar to 23, also showing cells being transformed into colloid.

## HORSE SERIES (continued).



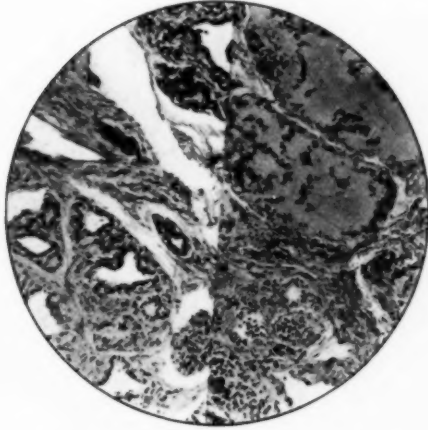
Section 25.—Left, active hyperplasia serum, low antitoxic value. Right, hyperplasia being changed to colloid, higher antitoxic value of serum.

## TUMOUR SERIES.



Section 26.—Left, hyperplasia from exophthalmic goitre. Right, hyperplasia from eleven days' measles.

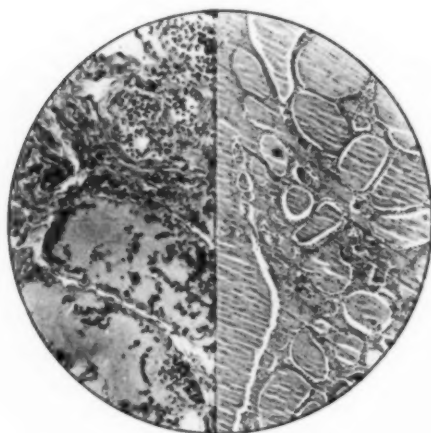
TUMOUR SERIES (*continued*).



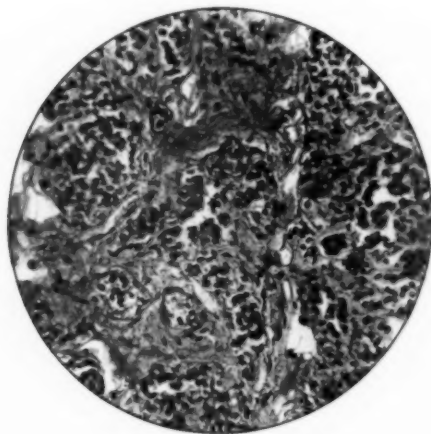
Section 27.—Left, hyperplasia from thirty-seven days' whooping-cough. Right, involution to colloid gland three months later.



Section 28.—Left, hyperplasia from active Graves's disease. Right, its involution to colloid gland.

TUMOUR SERIES (*continued*).

Section 29.--Left, involution to colloid after whooping-cough. Right, involution to colloid after exophthalmic goitre.



Section 30.—Fœtal thyroid. Condition corresponding to hyperplasia.



## **Pathological Section.**

November 19, 1912.

Dr. R. T. HEWLETT, President of the Section, in the Chair.

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### **Remarks on Further Experiments concerning the Origin of Life.**

By H. CHARLTON BASTIAN, M.D., F.R.S.

My work, entitled "The Origin of Life," was based in the main on 196 experiments with hermetically sealed tubes whose contents had been exposed to high temperatures. Since the date of its publication in the spring of 1911 I have performed a much larger series of experiments—as many as 280—and consequently should be in a position entitling me (1) to pass some judgment on the value of my previous results; (2) to deal more or less authoritatively with the doubts expressed by others as to the validity of my conclusions; and (3) to offer some useful advice to those who may wish successfully to repeat my experiments.

#### **(I) The Nature of the Problem, and the Extent to which it has been solved.**

It has long been widely believed in the world of science that the occurrence of "spontaneous generation" is a myth. This view gathered strength thirty to forty years ago, seeing that the experiments of Pasteur, and later those of Tyndall, induced them to urge it with much insistence; and because, moreover, it has seemed to be in accord with the practice found needful in bacteriological inquiries of growing importance. In all their experiments Pasteur and Tyndall,

as well as previous experimenters, made use of solutions of organic matter, mostly infusions of different kinds, heated to  $100^{\circ}$  to  $105^{\circ}$  C. for varying periods, and subsequently protected, more or less securely, from external contamination. All these solutions or infusions must have been more or less teeming with bacteria of different kinds, as well as with torulæ and germs of common moulds. This would have been notably the case with hay infusions, which were so largely used by Tyndall. These experimenters made no attempt whatever to exclude such organisms and their germs. They trusted to what was known and well established concerning the lethal influence of heat on living matter immersed in fluids, and consequently to their ability to sterilize the solutions and vessels used. Having extinguished all life in their media and receptacles, they exposed them for varying periods to what were considered suitable incubating temperatures. Then, if evidences of fermentation showed themselves within the experimental fluids, they were seemingly content to account for it as a result of some error; while their numerous negative results impressed them so strongly that they were induced to favour a general conclusion far wider than was warranted by their premises.

My own experiments have been of the same order, only much more stringent, seeing that instead of infusions of organic matter I have of late been dealing with saline solutions only—always contained in hermetically sealed vessels, and, moreover, often heated to temperatures very much higher than those employed by my predecessors. My saline solutions have also contained some bacteria, toruloid corpuscles and germs of mould, though probably very much fewer than those existing in the organic infusions dealt with by Pasteur and Tyndall, whose experiments have been believed to be so decisive.

Thus, if from the basis of their negative results they felt themselves warranted in proclaiming their belief that the present occurrence of "spontaneous generation" was a myth or chimera—a view which has been so widely accepted—how much stronger is my warrant for the opposite belief, looking to the very numerous occasions on which, when opening previously sterilized tubes and solutions, I have taken therefrom undoubted living organisms?

Even one such positive result free from all error is, of course, worth more than any number of negative instances. It will be well to consider, therefore, the various possibilities of error that have been suggested.

**(II) Reply to Criticisms.**

Some of my critics—mostly not biologists, and presumably not thoroughly acquainted with bacteria and torulæ—have supposed that what I have taken from my tubes have been mere pseudo-organisms, such as Leduc, Herrera, Jules Félix, the brothers Mary, and other plasmogenists are able to produce from various saline solutions—bodies which undoubtedly often simulate organic forms with great exactness. This, however, is an absolute error not likely to be shared by biologists,

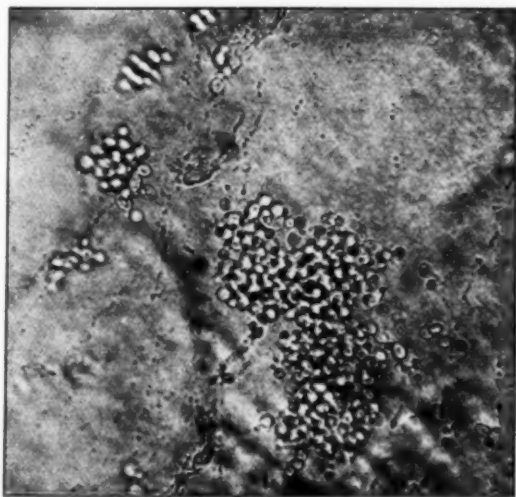


FIG. 1.

One of several groups of small torulæ beneath the same cover-glass, as taken direct from a tube containing a yellow solution, exposed to light, which had been heated seven months previously to 100° C. for twenty minutes on three successive days. ( $\times 700$ .)

and one which is shown to be erroneous by the fact of the free multiplication of my organisms when taken from their own media and introduced into other quite different nourishing fluids.<sup>1</sup>

Others do not doubt that the organisms found and photographed

<sup>1</sup> Solutions of 3 per cent. glucose and of 5 per cent. cane-sugar, as well as the ammoniac tartrate solution.

are real organisms, but cannot believe that they have really been engendered within the tubes. Some of these suggest that the organisms found have rushed into the tube from the atmosphere when its neck has been filed off. But there is practically no inrush of air at this time; certainly none that would suffice to carry atmospheric germs at once through the fluid (about  $1\frac{1}{2}$  in. deep) to the sediment at the bottom of the tube, where the organisms are always found.

Others suggest that the organisms may have been contained in the pipette; but this is always thoroughly heated in a spirit lamp flame just before it is introduced into the freshly opened tube. And when a small quantity of the sediment is obtained by the pipette, it is at once transferred to a thoroughly clean microscope slip and covered with a cover-glass.

Then torulæ are supposed by some of my critics to fall from the atmosphere on to the drop of fluid on the microscope slip during the moment or two that it remains uncovered. This supposed explanation, however, of the presence of organisms found by me is mere unsupported theory, as anyone would soon find who set himself to discover torulæ in the way suggested, and by an examination of fig. 1. That such formed organisms, and often in such numbers, could have been gathered from the atmosphere during the transit of the pipette for 1 or 2 ft. from the mouth of the tube to the microscope slip, and before the drop of the solution is covered, is, in fact, devoid of all probability; and will be shown to be so by the numerous cases subsequently to be referred to in which, during similar examinations of various series of other tubes (barren), no organisms whatever could be found.

Other critics are content to assume that the organisms found are not living. They believe them to be dead organisms—some of those pre-existing in the experimental fluids, but killed by the heat to which they and the tubes have been subjected. This objection requires to be looked at in more detail, because it is admitted that some few organisms may be found in the experimental fluids, derived from two of the constituents of such solutions—namely, the sodium silicate and the ammonium phosphate—the dilute phosphoric acid, the liquor ferri pernitrat, and the freshly distilled water being, however, free from them.

Any such pre-existing organisms would, of course, have been killed by the sterilizing process, but seeing that in each tube there would only be one to three drops of the dilute sodium silicate either alone (in the yellow solutions) or in association with 3 or 4 gr. of ammonium phosphate, as in the colourless solutions, these pre-existing organisms could

never be very numerous within the tubes. It is very important to note, moreover, that nothing like well-developed torulæ are ever to be seen in either of these newly prepared solutions. There are, however, often a few very minute spherical organisms (such as are shown in fig. 14 of "*The Origin of Life*") and, more rarely, a minute mould may be found when a "control" tube is opened, and some of the sediment is examined the day after the sterilizing process.

But let several months elapse, with suitable exposure to light or heat, before other tubes of the same series are opened, and then these minute "elementary organisms," as Professor Hewlett terms them, may be found in large numbers within the tubes, and staining freely

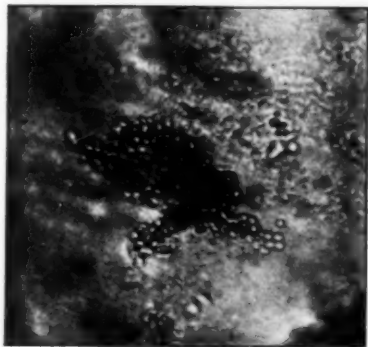


FIG. 2.

Large group of the elementary organisms taken from a tube containing a colourless solution which had been exposed to light for nine months after having been heated to 135° C. for five minutes. ( $\times 700$ .) Another sample of the sediment from this tube was ringed with paraffin, and after four days swarms of torulæ were found beneath the cover-glass.

with eosin or carbo-fuchsin. These primitive organisms are very slow and sluggish in their growth, requiring some months for origination and for their development from ultra-microscopic particles to the minute embryo bodies that are often so numerous, but which may not always be easily shown; to be living in the way that is open for torulæ and bacteria. Still, when tubes containing them have been closed, and then kept undisturbed for twelve months or so, they have often been found to have given rise to minute moulds, mostly of the *Streptothrix* type. The fact, however, that such minute organisms are either very scarce or

not to be found at all in control tubes, and to be abundant after months in other tubes of the same series which have never previously been opened, is conclusive evidence that they have developed and multiplied within the tubes. At other times, moreover, these "elementary organisms" are found to be associated with well-developed torulæ or with bacteria, which can be shown, in the course of a few days, to be living by the growth and multiplication which they undergo under the conditions indicated at p. 39 of "*The Origin of Life*," that is, either (a) by their multiplication on the microscope slip, beneath a cover-glass which has been ringed with paraffin; or (b) after their inoculation into certain nourishing fluids that have been previously sterilized. The so-called "elementary organisms" are, as I believe, to be regarded either as potential embryo torulæ or as fungus germs.<sup>1</sup> At times when they have been inoculated into a sterilized ammoniac tartrate nourishing solu-



FIG. 3.

Bacilli and a minute mycelium, stained with eosin, from a colourless solution which had been heated to 100° C. for twenty minutes on three successive days, and was opened after having been six months in an incubator, first at 27° C. and then at 37° C. ( $\times 700$ .)

tion swarms of full-grown, budding torulæ have been found after a few days; while when left in their own tubes at ordinary room temperature for many months minute moulds have, as I have said, been found within the tubes, one of which is shown in fig. 4.

Finally, other critics, unable from the evidence adduced to doubt that what I have taken from my tubes have been veritable organisms rather than mere pseudo-organisms; that they have really been taken

<sup>1</sup> Associated with them there can often be seen a number of particles of different sizes "down to the minimum visible stage," doubtless representing different stages in their growth and development. Precisely similar associations with growing torulæ were seen and described by me in "*The Beginnings of Life*," 1872, i, pp. 261-83.

from the tubes; and that they have been really living organisms, fall back upon the only remaining means of staving off the conclusion that they have been engendered *de novo* within the tubes. They hint darkly that some *desiccated germs* (hitherto unknown) may have been able to survive in the heating processes to which I have had recourse—though these have included exposures from five to twenty minutes to temperatures ranging from  $120^{\circ}$  to  $145^{\circ}$  C., or else the method vaunted by Tyndall as lethal for all desiccated germs, and now universally trusted by bacteriologists as a safe means of sterilization.

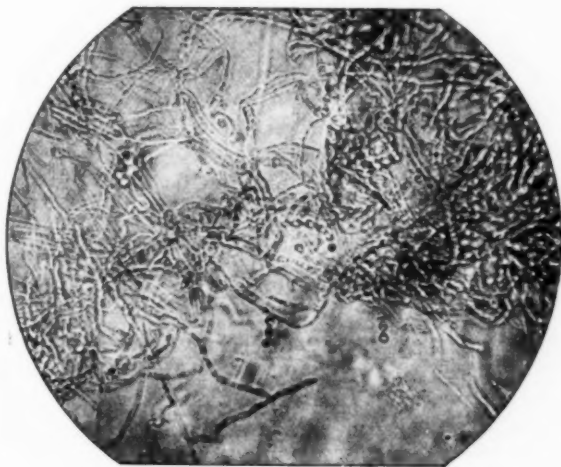


FIG. 4.

Mould from a colourless solution which had been heated to  $130^{\circ}$  C. for ten minutes in an autoclave five months previously to its being first opened, when numbers of the elementary organisms were found but no moulds. The tube was then securely closed and opened again after the lapse of twelve months, when numbers of small moulds of *Streptothrix* type were found on the flakes of silica, as well as a much larger mass, part of which is here shown. ( $\times 500$ .)

Strange that this objection should be raised now, seeing that my earliest results in 1870 were disbelieved in by Huxley, Burdon Sanderson and others because of the strength of their belief that bacteria and torulæ could not survive a heat of even  $100^{\circ}$  C. for a few minutes in fluids; and seeing that Pasteur himself never thought it needful to use a higher temperature than  $110^{\circ}$  C. in any of his experiments.



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This objection is, however, a sort of refuge of the destitute which has always played a large part in discussions concerning the *de novo* origin of life.<sup>1</sup>

But where are the obdurate desiccated germs imagined to come from, and why have they hitherto eluded discovery? They cannot exist in the yellow solutions which contain only about two or three drops of the dilute sodium silicate solution and four drops of the liquor ferri pernitratis to the half ounce of distilled water, yet it is precisely these particular solutions which I have found to yield a distinctly greater variety of organisms than the colourless solutions, into which desiccated germs might be introduced by the 3 or 4 gr. of ammoniac phosphate contained in each tube. Different kinds of mould have often been found in these yellow solutions, two of which are shown in figs. 5 and 6.

Any such doubt is, however, easily solved by introducing 5 or 6 gr. of this salt into 1 oz. of the sterilized ammoniac tartrate nourishing solution, and boiling it merely for five instead of twenty minutes on three successive days. Treated in this way ammoniac phosphate crystals cannot be shown to contain living organisms capable of resisting even such comparatively low temperatures and short exposures, though the tubes may have been kept under favourable conditions even for seven or eight months. And that the suggestion is groundless in the present case is shown by the fact to which reference has been made on p. 60 touching the barrenness of tubes when their solutions have been made from old samples of sodium silicate or colloidal silica, though these solutions can be easily shown (by inoculation) to be still capable of favouring the free growth and multiplication of organisms.

Further, it must never be forgotten that torulæ and micrococci, which have so frequently been taken from the tubes (and more especially the former), are not known to be capable of resisting temperatures even of 60° to 70° C. for two or three minutes.

<sup>1</sup> After what has been stated on p. 58 (loc. cit.) concerning the sterilization of the tubes employed, no one has ventured to renew a previous objection and say that the experimental vessels have not been sufficiently *flambés*. All germs on the tubes, when nearly red hot, would have been effectually burned off.

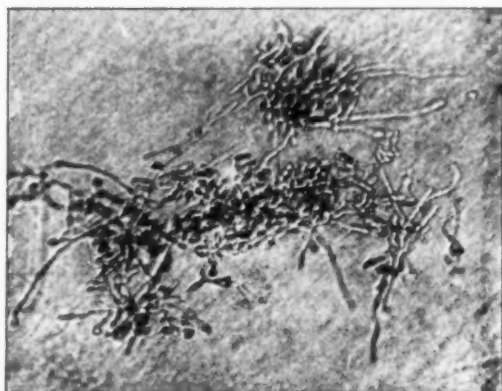


FIG. 5.

Mould of *Streptothrix* type as taken from a tube containing a yellow solution, which after having been heated to 100° C. for twenty minutes on three successive days, was exposed to light for seven months. ( $\times 300$ .)

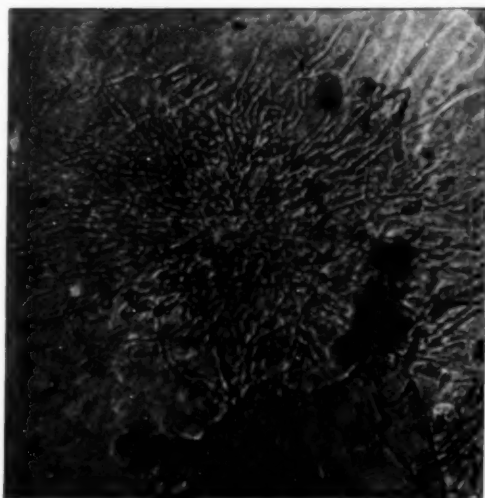


FIG. 6.

Part of a much larger mould of the same type as the last, as taken from a companion tube which had been similarly treated and similarly exposed to light for seven months. ( $\times 300$ .)

## (III) Concerning the New Experiments and what should be done in further Trials.

(A) *Exposure to Daylight or in the Incubator.*

One of the first points as to which I needed further information was the extent of exposure to direct sunlight that was advisable.

As related (*loc. cit.*, pp. 50, 56), I had found that exposure of the tubes inside a south window during the last three to four weeks, before the opening of them, was followed by good results; though I was always rather doubtful whether this was not merely due to the increased heat to which they and the solutions were thus subjected.

In the spring and summer of 1911 a number of tubes were exposed from the first inside a south window, the weather being unusually bright and warm during most of the time. The result was that when the time came for their examination the solutions were found to be nearly all barren. As I subsequently ascertained that the temperature of the window ledge on which the tubes stood rose often daily for some hours to 43° C., or even rather higher, I am disposed to think that the harm was probably more due to the prolonged and repeated high temperatures than to the effect of the mere actinic rays through the thick window glass and that of the tubes. In view of this experience I now advise that all tubes exposed to light should be placed just inside a north or, better still, a north-east window; unless they can be put into a conservatory, and protected there from the direct rays of the sun.

Tubes exposed to light should not be examined till nearly six months have elapsed, in summer; or eight to twelve months when much of the time of exposure has been in colder and duller weather. During winter months I have, however, of late made use of the incubator, maintained at 27° and at 37° C., and I prefer half of the time to be at the lower and half at the higher temperature. I cannot say positively at present whether it would or would not be desirable to use the higher temperature from the first; though I have found that a final temperature approaching 43° C. for two weeks has been distinctly harmful, often apparently killing plenty of torulæ, found when the tubes were opened.<sup>1</sup> Exposure to such a high temperature from the first, therefore, would

<sup>1</sup> On two or three occasions they have really been very numerous, but apparently dead, as no evidence of subsequent multiplication could be obtained. It looked as if growth and multiplication had been at first stimulated, and that the continuance of the high temperature had ultimately killed the torulæ.

probably prevent the evolution of organisms, and thus would explain the barrenness of the tubes that were exposed from the first to the hot sunlight of 1911. Tubes exposed in the incubator should not be opened under four to six months.

(B) *New Combinations Tried.*

As the organisms were often so scarce in the experimental solutions, and this might be considered due to the scarcity of carbon within the tubes, I made a series of tentative experiments trying to remove this disadvantage; as a result of which I found that the colourless solutions could be varied by the addition (to each fluid ounce containing the ordinary constituents) of 4 gr. of neutral ammonic tartrate with 2 gr. of sodic phosphate; and also by the addition to each ounce of 4 gr. of ammonic carbonate, or 6 gr. of pure glucose. Trials with the first of these more complex solutions yielded torulæ with one sample of sodium silicate, but not with another; though the organisms were not notably more abundant than they had previously been found to be in a similar solution without the additions indicated. Those in which ammonic carbonate was added have all been barren; and those with the addition of glucose have also all been barren. In the latter case, however, the solutions were unfortunately made this spring with some of an old sample of sodium silicate.<sup>1</sup> Further trials with the addition of glucose ought therefore to be made. None of these additions could be made to the yellow solutions without causing their complete decomposition.

Another variation in the solutions with which trials have been made has been the substitution of Kahlbaum's 10 per cent. sodium silicate for one of the ordinary commercial preparations. This was used in the proportion of fourteen drops to the ounce for the colourless solution, and seven drops for the yellow solution—the quantities of the other ingredients being in each case those usually employed. But in all these trials the solutions have either been almost barren, or have only yielded bodies of an uncertain nature. Torulæ have never been found in either of them, though in the yellow solutions what appeared to be large sausage-shaped bacilli were taken from three tubes of the same series.

<sup>1</sup> Though the tubes were opened after they had been in the incubator for six months no organisms of any kind could be found. I then inoculated each of the tubes with three drops of a turbid ammonic tartrate solution and replaced them in the incubator. At the expiration of only *two days* each fluid was slightly turbid and swarming with bacteria.

It seems clear, therefore, that in the ordinary commercial sodium silicate additional elements must be present that are not found in the 10 per cent. solution, and which, in some way, help to favour the evolution of living units.

(C) *Preparation of the Solutions.*

A very important point has only lately been thoroughly brought home to me, which is, that too old solutions of sodium silicate must not be employed. I have carefully kept the solutions obtained in the spring of 1910, not only with the view of myself repeating combinations which I had previously found successful, but in order that I might give others, desiring to repeat my experiments, some of the actual materials used by me.

During the present year solutions prepared exactly as they had been in the previous summer and earlier have no longer been yielding torulæ and bacteria as of old. I found first that the yellow solutions, made exactly as they had been before, became decomposed, and that the colourless solutions which, after the heating process, should have yielded a slight amount of deposit showed none at all. Thus many tubes were spoiled. And when, by slight alterations in the number of drops of the dilute sodium silicate for the colourless solutions, I succeeded again in producing a scanty deposit after heating, even then, after due exposures either to daylight or in the incubator, no torulæ were found when the solutions came to be examined. The deposit itself, moreover, had often not the same character as of old. These irregularities caused me much perplexity at first, but I have now come to the conclusion that they must be due to changes which have taken place in the stock supplies of sodium silicate that I have been using since the spring of 1910. That these have undergone some change is now indeed obvious, since at the bottom of each bottle there is a white, cloudy deposit nearly an inch in depth, which has been gradually increasing. This was comparatively unheeded by me, as when using either of the solutions I had been accustomed to withdraw with the pipette only some of the clear supernatant fluid.

Several times during this year solutions that I have prepared, exactly like those which formerly yielded a fair amount of torulæ, have proved, after similar exposures, to be so barren that not a single torula could be found. I had not suspected this kind of degradation with the ordinary commercial sodium silicate, though I had nine months ago recognized

that the dilute colloidal silica with which I was so uniformly successful in 1910 had in some way lost its virtues, seeing that the next time I used it, after an interval of eight months, solutions similarly prepared and similarly treated no longer yielded torulæ as before. I looked upon this as a well-known unstable fluid, liable to undergo change; but had not suspected that the commercial sodium silicate might also, though after longer periods, undergo changes and similarly become less productive when used as a constituent of one of the previously fertile solutions.

How soon the colloidal silica undergoes these harmful changes I am at present unable to say, but I am afraid it does so even in the course of a few months. In his original description Professor Graham said<sup>1</sup>: "Another and eminently characteristic quality of colloids is their mutability. Their existence is a continued metastasis. . . . The solution of hydrated silicic acid, for instance, is easily obtained in a state of purity, but it cannot be preserved. It may remain fluid for days or weeks in a sealed tube, but it is sure to gelatinize and become insoluble at last. . . ."<sup>2</sup> To the gradual manner in which colloidal changes take place (for they always demand time as an element) may the characteristic protraction of chemico-organic changes also be referred."

Dr. Rosenheim was kind enough to prepare and give me a new supply of the very dilute colloidal silica last November, and a few tubes were at once charged in which it was one of the constituents. Two of these were examined after they had been only five and seven weeks respectively in the incubator, and no torulæ were found after these short periods; while two others were opened after thirteen weeks, one of which had been in the incubator and one exposed to light, and in each of these latter tubes a moderate number of typical torulæ were found. Other solutions were made with it barely four months after it had been received. Two of these tubes were examined after seven weeks and no torulæ were found. While others were recently examined after four to seven months, and they also, much to my surprise, have been barren. I fear, therefore, that this new supply of colloidal silica had already undergone some harmful changes even after the comparatively short period of four months.

The fact of the barrenness of solutions in which old samples of commercial sodium silicate, or not quite fresh solutions of colloidal

<sup>1</sup> *Phil. Trans.*, 1861, cli, p. 183.

<sup>2</sup> The solution I have been using is so dilute that it never actually gelatinizes.

silica, had been used is of itself a convincing proof that the temperature to which these and other tubes have been submitted has sufficed to kill any organisms that the solutions may have originally contained; while the fact that organisms are much more abundant in these old stock solutions than they are in fresh supplies, and that they go on increasing in them, shows that their capability of favouring mere growth and multiplication of such organisms is in no way diminished. The remainder of my stock solution of colloidal silica is clear like water, but there is now a slight sediment which on examination is found to be composed of bacteria, toruloid corpuscles, fungus germs and minute moulds. Numbers of such organisms may also be found mixed with the white deposit in the bottles in which the old commercial silica has been standing.

I have, moreover, inoculated the barren solutions, in many of the tubes of which I have been speaking, with organisms taken from the old stock supplies, or with others growing in a contaminated ammoniac tartrate solution, and have found that the organisms grew and multiplied freely in these previously barren tubes, thus showing that it was not the power of nourishing organisms which had been lost in the solutions made from the old supplies, but what, owing to some change, we can only regard as the capacity for engendering them. It also explained what for a time was a great puzzle to me, that is, why solutions precisely alike in their constitution and the conditions to which they had been subjected should at first be fertile and then, when prepared at a later date, should be barren.

From what I have said, it seems clear that it is better not to work with ordinary commercial sodium silicate which is more than twelve months old, and that the dilute colloidal silica used should be only recently prepared.<sup>1</sup> It must be recognized also that no two samples

<sup>1</sup> Looking to the uniformly successful results that I obtained when working with the freshly prepared, very dilute colloidal silicic acid, it is much to be desired that others should repeat these particular experiments. Dr. Rosenheim has kindly sent me the following details concerning the mode in which, by a modification of Graham's method, he prepared the weak solutions, samples of which were given to me: "66 c.c. of Kahlbaum's sodium silicate (10 per cent.) were diluted to 200 c.c. with distilled water, and the solution was poured into an equal volume of water containing 20 c.c. of concentrated HCl." "A specially prepared appendix from a sheep (see 'Handbuch der biochem. Arbeitsmethoden,' E. Abderhalden, iii, p. 10) was filled with the slightly opaque solution and suspended in the dialysing apparatus of Wiechowski (see *ibid.*, iii, p. 177). Dialysis against running distilled water was carried on for ten days until the dialysate was perfectly free from chlorides." The first sample given to me was, according to Dr. Rosenheim, "a pure 0.01 per cent. solution of colloidal silica" (see "The Origin of Life," p. 52, note 2). Kahlbaum declined to supply any such solution, partly because of its instability.



are exactly alike,<sup>1</sup> so that in order to estimate the amount of the dilute sodium silicate to be used when dealing with a new supply tentative trials must be made, as described at p. 30 of "The Origin of Life"; the aim for the colourless solutions being to obtain only a quite small amount of deposit after the fluid, boiled for ten to twenty minutes, has been subsequently cooled; while for the yellow solution, when cooled, the aim should be to obtain also a minute amount of deposit from a fluid having a pale port wine colour, or else (when the amount of the silicate is at times only very slightly more) a pale canary-yellow colour.

After trials of this kind have been made the worker will know how many drops of the dilute sodium silicate with which he is dealing should be used to the ounce for the yellow and for the colourless solutions respectively; and he may be fairly certain that the results will be similar for the hermetically sealed tubes after the sterilizing process if they have been charged with similar solutions.

In the actual preparation of the fluids a certain order should be observed. Thus, for the yellow solution it is important that the liquor ferri should be added to the distilled water first, and then the dilute silicate drop by drop.<sup>2</sup> For the colourless solutions I have of late been dissolving the ammoniac phosphate and filtering the solution first, through the finest (No. 0) Swedish filtering paper, to remove minute impurities

<sup>1</sup> Quite recent experience leads me to think that the commercial product is now more variable than ever, owing perhaps to the fact that it is no longer much used by surgeons. Samples that have lately been supplied to me have varied very much, so that it is more than ever important to make use of recently prepared pure colloidal silica. (November 23, 1912.)

<sup>2</sup> Reversing the order generally leads at once to the formation of a dense precipitate. And the changes, with different quantities of sodium silicate added at the proper time, are often very surprising, as may be seen from the following example of the results obtained in the testing of a new supply of sodium silicate. In each trial eight drops of the iron solution were used in an ounce of water, and when the one or more drops of sodium silicate had been added, the solutions were boiled for fifteen minutes and then allowed to cool. The results, with different proportions of sodium silicate, were as follows:—

- |           |   |
|-----------|---|
| 1 : 8 ... | Fluid colourless. Deposit red and copious.                        |
| 3 : 8 ... | Fluid slightly yellow. Deposit red and copious.                   |
| 5 : 8 ... | Fluid reddish-yellow. Deposit reddish-yellow and copious.         |
| 6 : 8 ... | Fluid yellow and slightly clouded. Deposit very minute in amount. |
| 7 : 8 ... | Fluid yellow, not clouded. Deposit moderate in amount.            |
| 8 : 8 ... | Fluid of pale drab colour. Deposit drab and copious.              |

This sample of sodium silicate would not yield the port wine colour of solution such as I had often obtained with other samples. With another supply tested on the same day the results were equally variable, but different. In charging tubes with some of the supply, results with which are given above, I used a 6 : 3 solution, as the deposit with time tends to increase slightly.

that may be found with the crystals, before adding the dilute phosphoric acid and then the dilute sodium silicate.<sup>1</sup>

Of late, in order to be able to pursue these studies where I live, in the country and away from a laboratory, I have been boiling the tubes for twenty minutes on three successive days rather than heating them as before to higher temperatures in an autoclave or an oil-bath.

(D) *Examination of the Solutions.*

When examining the solutions I use a pipette about 8 in. long, having a bore of 3 mm. and provided with a rubber teat at its expanded upper extremity. It is desirable to take up with the sample of sediment only a single drop of the fluid, so that when this sample is transferred to the microscope slip it may be kept together under a carefully lowered cover-glass. The specimen is then systematically searched through, beginning at one side of the cover-glass and working regularly up and down till the whole field has been carefully examined, at first with a  $\frac{3}{4}$ -in. objective, or concurrently with that and a  $\frac{1}{8}$ -in. with No. 6 eyepiece, and all the time using the nose-piece freely, so as to bring the higher power into use when anything like an organism comes into view. This answers well for the detection of torulæ, but of course for bacteria only the higher power is of any use.

The light in all cases requires to be most carefully adjusted so as to get the right kind of illumination, and when the organisms are scarce and minute their recognition may be much facilitated by running under the cover-glass a drop of a freshly filtered solution of eosin or of carbo-fuchsin.

CONCLUSION.

There is one difficulty of a general character applicable to all experiments of this order, though not more to mine than to those of previous workers, to which it may be well to make reference here.

<sup>1</sup>In some experiments made in conjunction with Sir William Ramsay and Dr. A. C. Stevenson, both colourless and yellow solutions were centrifugalized for twelve hours or more in order to get rid of any organisms that the solutions might contain. The tubes charged with these solutions, after having been sealed, were boiled for twenty minutes on three consecutive days. Several of these tubes, which had been in the incubator for over six months, have lately been examined, with the result that they have been found to contain bacteria, torulæ, and moulds just as freely as in other similar solutions which had not been centrifugalized.

Many persons find it more or less impossible to believe that bacteria, torulæ and simple moulds should be products of the so-called spontaneous generation, and that for two reasons.

In the first place, they are not deemed simple enough to rank as primordial living things. But what has been said on this head by others of late makes it desirable for me to repeat what I have often said before, namely, that new-born living matter, wherever and whenever it appears, must have its first beginnings as ultra-microscopic particles, which as they grow would at last become recognizable by the aid of the microscope as very minute spherical units.<sup>1</sup> These may in some cases go on to the formation of micrococci, of bacilli of different kinds, of torulæ, or of germs which gradually develop into one of the simplest moulds. When it is said, therefore, that such organisms are not simple enough to be regarded as primordial living things it must not be forgotten that the real primordial formations are ultra-microscopic particles, and whatever the type produced, whether minute formless masses of jelly, like the monera of Haeckel, or blue-green algoid corpuscles, they also would in each case have to commence as ultra-microscopic particles.

It seems to me quite possible that in Nature both monera and blue-green algoid corpuscles may be constantly appearing *de novo*.<sup>2</sup> But that is a mere supposition devoid of all positive evidence, as it must always remain till someone may be fortunate enough, whether chemist or biologist, to hit upon such combinations of materials as will, under necessarily restricted experimental conditions, suffice to engender either monera or blue-green algæ. For whatever the future researches of chemists may achieve in the way of synthetically building up the bases of protoplasm, when it comes to the demonstration of the production of actual living matter, they could never convince themselves or the world in general that they had succeeded in their quest till they were able to produce it under such restrictive conditions as I have had to cope with

<sup>1</sup> When it is said, therefore, that a belief in "spontaneous generation" would tend to contradict the experience of all mankind, "my reply is that archebiosis may be occurring all around us, and that from its very nature it must be a process lying altogether outside human experience and never likely to come within the actual ken of man" ("The Nature and Origin of Living Matter," 1905, p. 144); while long previous to this, in "The Beginnings of Life," 1872, i, p. 267, I described what I then termed "plastide particles" (rather than "microzymæ") as primordial particles of living matter "between  $\frac{1}{100000}$  in. and  $\frac{1}{20000}$  in. in diameter"; and at pp. 293-297 I described the mode in which such particles might be seen to emerge in certain solutions from the region of the invisible and gradually develop into bacteria.

<sup>2</sup> "The Nature and Origin of Living Matter," p. 145.

in my experiments, that is, within hermetically sealed vessels which with their contents had previously been sterilized. They, like the biologist, would have to eliminate all pre-existing life, and securely guard against contaminations, and what the chemist may then produce as a result of new combinations no one can say, though he is certainly never likely to produce living matter in tangible lumps, as recent vaticinations in regard to what "the chemist is going to do in his laboratory" would seem to intimate. It may be safely affirmed that living matter, like crystalline matter, must always begin from a collocation of its elements, and can then only after a time reveal itself as minutest particles tending to develop in this or that manner in accordance with the extremely varied nature of the initial molecular combinations; and for our sterilized solutions we can only suppose that the conditions are such as merely to permit of the production of ultra-microscopic particles that slowly in the course of months (rather than in a few days, after the manner of infection by pre-existing organisms) develop into bacteria and torulæ, though the latter have the potentiality of growing into simple moulds.<sup>1</sup>

What real knowledge, however, have we entitling us to come to any definite opinion as to what primordial living things should or should not be like? We know, indeed, that primordial crystals may be either simple or of very complex forms. Rather let us be content carefully to question Nature by way of experiment, and learn from her to think less of the other objection to bacteria and torulæ being accepted as veritable products of spontaneous generation, that is, simply on the ground that they are well-known forms instead of being something new and strange. This latter one-sided objection, strongly raised by Huxley in 1870 in an address "On the Relations of Penicillium, Torulæ and Bacterium,"<sup>2</sup> would necessarily disappear with the proof of "spontaneous generation," because then it would at last be realized that what took place in the experimental vessels must be much more freely occurring

<sup>1</sup> As long ago as 1868, M. A. Trécul, an eminent French authority, in an important article entitled "Observations sur la levûre de bière et sur la *Mycoderma cerevisia*," *Compt. Rend.*, lxvii, pp. 137, 212, 1153, brought forward very conclusive evidence tending to show that *Torulæ cerevisia*, *Mycoderma cerevisia*, and *Penicillium*, as he says, "ne constituent qu'une seule espèce" (since these forms were shown to be mutually convertible), and moreover, that torulæ, under the conditions which he described, were constantly arising *de novo*—showing themselves first as minutest particles. See also the investigations of Hector Grasset ("Etude historique et critique sur les Générations spontanées et l'Hétérogénie," 1912, 2nd ed., pp. 157-59) for further light on these subjects, and a simple means of proving the *de novo* origin of torulæ within the grape.

<sup>2</sup> *Quart. Journ. of Micros. Sci.*, 1870, n.s. x, p. 355.

in the world outside, and that the bacteria, torulæ and moulds, whose appearance is so ubiquitous, must be constantly originating as well as multiplying all around us. We should, moreover, no longer have to postulate the existence everywhere in the atmosphere of inconceivably numerous and varied germs, always ready suitably to tenant every new possibility in the way of site, however unusual it may be.<sup>1</sup> To meet such requirements the atmosphere ought to present itself as infinitely more crowded with germs of the most varied kinds than it has ever been found to be by the many persons who have most carefully examined it from this point of view.

### Some Points concerning the Vaccine Treatment of Gonorrhœa and the Regulation thereof by the Complement-fixation Test.

By J. E. R. McDONAGH and B. G. KLEIN.

THE work which has been done with the Wassermann reaction in connexion with the diagnosis of syphilis and the regulation of the treatment thereof prompted us to apply the knowledge gained therefrom in order to ascertain whether parallel results could be obtained in gonococcal systemic infections. Our technique of the complement-fixation test did not depart in any way from the original, but we found it wiser to employ a little stronger solution of complement than is required for the Wassermann reaction owing to the avidity for fixing complement which most bacillary emulsions possess. We also used the patients' sera diluted 1 in 5 instead of 1 in 10, so as to avoid overlooking a serum which only contained a little antibody.

The antigen being the most important part of the experiment requires special consideration. Only twenty-four to forty-eight hours cultures on freshly prepared ascitic fluid or pleural fluid agar were used. The resulting growth was emulsified in normal saline containing 0.5 per cent. phenol, and the strength of the emulsion found, by counting against normal blood according to Wright's method. As a rule 300 to 500 million per cubic centimetre were about the limits between

<sup>1</sup> See Fée as cited by Hector Grasset (*loc. cit.*, I. Rousset, p. 37), and a much longer list given by Pouchet ("*Hétérogénie*," 1859, pp. 336-39) of rare moulds found (but with constancy) only in rare and exceptional situations.

which the strength of the emulsion was adapted to the successful working of the test. We employed altogether fifteen different strains of gonococci and were always careful to use only those emulsions prepared from the original culture, or first subculture, as those obtained from lower subcultures give indifferent results. The emulsions, if required for further use, should be stored in the dark at 0° C. Under these conditions they appear to remain little impaired for ten days, but then they begin to lose their power of combining with the specific antibody. In this respect different strains vary, as one of our emulsions retained its antigen properties for considerably longer.

In every series of tests one known positive and one known negative sera were included. For the latter we tested altogether from thirty to forty sera of normal persons and of patients suffering from diseases other than gonorrhœa, but in no single case was any fixation of complement noted. For the former we employed a serum with which we had already obtained a triple plus, and in addition we used Burroughes and Wellcome's antigonococcal serum, which was obtained from a horse which had been immunized with subcutaneous injections of cultures; with such a serum a triple plus result was invariably obtained in dilutions up to 1 in 10. Sera remain active for at least a fortnight if kept undiluted in the dark at 0° C. in sealed pipettes, but after a time they become amphoteric, a property which can sometimes be destroyed by re-inactivating for half an hour to an hour.

Differences exist between the several strains of the gonococcus as regards their capacity for fixing complement in the presence of the specific amboceptor, so it occurred to us to inquire as to whether these differences related to the nature of the gonorrhœal infection from which the strain was isolated. One of our best strains both as regards its antigen and vaccine properties was obtained from a case of acute anterior urethritis, which was cured in ten days with injections of potassium permanganate as the sole treatment. On the other hand, an antigen prepared from a culture from the heart's blood of a fatal case of gonococcal septicæmia was by no means so active. Again, one strain was grown from a subacute case of urethritis in a male of average severity; the culture was not by any means abundant, but was undoubtedly the true gonococcus. The emulsion of this culture failed entirely to fix complement in the presence of a known triple plus serum.

It appears to be the case, therefore, that no definite relation can be traced between the nature of the case from which a strain of gonococcus is derived and the properties of this strain as tested by the com-



plement-fixation test. Such a conclusion is quite in harmony with the known facts with regard to the relative virulence of strains of the diphtheria bacillus or the typhoid bacillus. For example, strains of the diphtheria bacillus from such a mild affection as membranous rhinitis have been shown to have a marked virulence when injected into guinea-pigs. Hence it may be inferred that the relative virulence of any given strain of the gonococcus is not the chief factor in determining the severity or mildness of the infection. There must be other factors, such, for example, as the resistance of the infected individual, the site of entrance of the micro-organism (the different streptococcal diseases produced by the *Streptococcus pyogenes* according to the path by which it finds an entrance into the body), and the quantity of the virus which is implanted upon the host. It likewise shows that a vaccine prepared from a strain obtained from a severe case will not necessarily be a potent one.

Our next step was to try to determine the relationship between an emulsion as an antigen in the complement-fixation test and the same emulsion as a vaccine. An emulsion of gonococci is an "antigen"—i.e., contains the bacterial bodies and endotoxins which when inoculated into the living organism give rise to the formation of a specific antagonistic substance or antibody. The term "antigen," perhaps unhappily, is also commonly used to denote that factor in the complement-fixation test which combines with the antibody. The term in both cases is applied to the same thing, the bacterial emulsion, but to two different effects of it, one manifested in the living organism, the other in the experiment *in vitro*. Nevertheless, it is a probable inference that an emulsion of bacteria which has a high antigen value in the test *in vitro* will also have a high antigen value when injected into a living animal or patient. We have found in practice that the emulsions which most completely fixed complement (in the presence of positive sera) were most likely to provide potent vaccines: therefore gonococcal vaccines can be standardized by determining their antigen value *in vitro*.

A curious phenomenon encountered may be briefly alluded to in this place. One of the patients whose serum was repeatedly examined was a man, A. K., aged 22, suffering from severe gonorrhœal arthritis of many joints. His serum at intervals of over a month always gave a triple plus with several antigens, with one exception—viz. the strain of gonococcus isolated from his own urethra after prostatic massage. With this strain the fixation of complement was incomplete.



## VACCINES.

All that has been said of our method of obtaining the cultures, making and counting the emulsions for the antigen in the complement-fixation tests, applies to the preparation of vaccines; in fact, many of the strains were used for both purposes. Emulsions intended for use as vaccines were, however, autolysed for twenty-four hours at 37° C. to kill the gonococci. No heat was employed. The gonococcus rapidly autolyses at blood heat, and no living cocci remain at the end of twenty-four hours.

Three methods of vaccine treatment were employed and regulated by the complement-fixation test.

*(I) Vaccines injected Subcutaneously in the usual way.*

*Therapeutic Effects.*—Such vaccines we found rarely failed to produce a certain reaction, sometimes a marked reaction, even in the moderate doses we employed. We should not have been prepared to inject them in the large doses sometimes advocated, and are inclined to believe that the stock vaccines which can with impunity be employed in doses of several thousand million must be either old preparations or made from strains attenuated by repeated subculture. We did not use autogenous vaccines. In the chronic cases with arthritis, which formed the bulk of our cases, such a proceeding was difficult, if not impossible. In general we are of opinion that it is far more important in gonorrhœa to use a vaccine *recently made from an original culture or first subculture* than to lay a great stress on the vaccine being autogenous. Two preparations on the market were also employed for subcutaneous infection—viz., “gonargin” and “arthigon.” Tested by the complement-fixation test method gonargin showed the presence of antigen, though not to anything like the extent to which it was present in our freshly made emulsions. Arthigon had very feeble properties as a vaccine, and in the complement-fixation test no definite result could be obtained unless the emulsion was so diluted as to make the test valueless. The emulsion *per se* fixed complement to an extraordinary degree, so that we made little use of the “arthigon” preparation for treatment, for the above reasons. An increase is produced temporarily in the discharge in many cases with all the ordinary subcutaneous vaccines we have employed, and this temporary increase tends to diminish with each succeeding injection. A negative phase almost

invariably occurs after every subcutaneous injection, and its duration depends upon the dose used and the interval which elapses between each dose. One case was given 50<sup>6</sup> gonargin on three successive days, with the result that the complement-fixation test did not return to positive as it was before the first dose was given for three weeks, during which time the discharge increased and the epididymitis lighted up again. If, then, vaccines are to be used subcutaneously, or, better, intramuscularly, as by this route the local reaction is prevented, only small doses should be employed and longer intervals should be allowed between the succeeding injections, than is generally advised. The dose should range from 5 to 10 million, and should not be repeated for a fortnight or even longer; then each future interval can be gradually shortened as the duration of the negative phase diminishes.

#### (II) Intravenous Injections of Vaccine.

Having ascertained how to obtain active vaccines for subcutaneous injection, our next experiments were directed to the use of them *intravenously*. We made use of an autolysed emulsion containing originally 1,000 million gonococci per cubic centimetre. It had been kept in a sealed tube at 0° C. for more than three weeks. On centrifugalization the amount of deposit was very slight. A comparatively old emulsion was purposely preferred to a more recent one, as being more completely autolysed and containing more of the active principle *in solution*. Obviously, it might not be thought advisable to inject intravenously an emulsion containing bacterial bodies, even though dead. The supernatant fluid was pipetted off and ascertained by culture to be sterile. It was then tested for complement fixation in the presence of a known triple plus serum. Compared with a recent emulsion, which we had in use at the time, it had lost some of its power, but retained sufficient to justify its use as a vaccine. We therefore started to use it in comparatively large doses—viz., 5 million. In diluting down, the fluid was reckoned as equal to 1,000 million per cubic centimetre, and the smaller doses calculated accordingly. Each injection was given in 5 oz. of saline, as by using a large bulk of fluid a more general distribution would be achieved.

*Effect of Injections.*—The above sterile fluid injected subcutaneously in doses of 10 million was followed by little reaction and good therapeutic effect. Intravenous injections in smaller doses produced no reaction, and the beneficial effect was marked, even in doses of 1 million. It is not necessary to exceed a dose of 20 million. Probably, even with

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5 or 10 million, as good results are obtained. The doses we used were probably too big. It might be better to start with 1 million and then gradually increase by 1 million weekly. Contrary to what might be expected, the negative phase is negligible (judged by clinical signs and the serum reaction) after intravenous vaccine, provided not too big a dose has been given. In this respect intravenous vaccines are preferable to subcutaneous.

*Effect on the Patient's Serum as shown by the Fixation of Complement.*—The patients treated by the intravenous injection of vaccine were mostly those who had given a strong positive reaction in the complement-fixation test. Following the injections the reaction underwent variations, very much in the way that the serum reaction is changed in syphilis by salvarsan. During the course of intravenous vaccine injections the positive reaction in favourable cases becomes less positive, sometimes returns for a time to a strong positive, and again becomes yet more diminished in intensity, until finally it becomes negative. The average number of injections required to obtain a negative reaction is about ten. Sometimes even that number is insufficient. If too big doses are given the complement-fixation test becomes negative, but the symptoms are aggravated, and when the latter have quietened down the reaction becomes positive again.

### (III) *Sensitized Vaccines.*

*Preparation of the Sensitized Vaccine.*—This was carried out according to the method recommended by Besredka. The bacterial emulsion of a fresh living culture is counted. It should be of strong emulsion (never less than 1,000 million per cubic centimetre). To a measured amount of this (2 c.c. for example) about 1 c.c. of the immune serum is added. (Besredka prefers to use as little antibody as is compatible with sensitization.) The mixture is left at room temperature for twelve hours, by which time the bacteria are deposited at the bottom of the tube. The serum is now pipetted off and replaced with saline. The tube is shaken and then centrifuged. The saline is then pipetted off and replaced by more, and the tube again centrifuged. The deposit of bacteria washed free of serum is finally made up to the original bulk with 0.5 per cent. phenol saline, and this constitutes the sensitized vaccine.

## THE IMMUNE SERUM USED IN SENSITIZING.

*(I) Immune Horse Serum.*

Burroughes and Wellcome's antigonococcus serum, the serum of a horse immunized by subcutaneous inoculation with several strains of gonococcus. This serum gave complete fixation of complement; it was used, as already mentioned, as one of our triple plus controls. It contained much antibody, therefore it was reasonable to suppose that it was well adapted to the preparation of a sensitized vaccine. This expectation, however, was not realized. The first experiments we made with this sensitized vaccine were unsatisfactory. Local reactions were not pronounced; improvement was noted in the joints or other foci of infection, and no negative phase occurred; but bad general effects were produced, the patients had diffuse pains and felt ill, and rises of temperature occurred.

*(II) Human Immune Serum.*

In consequence of these bad effects we decided to continue with sensitized vaccine, but in preparing it to use for immune serum human serum taken from the vein of a gonorrhœal patient. Such a serum was obtained from a case taken at a time when it gave a strong positive result in the complement-fixation test subsequent to six intravenous injections of the autolysed vaccine with doses at weekly intervals of 5 to 20 million. The sensitized vaccine made with this serum behaved very differently from that prepared with the immune horse serum. Not only did the symptoms of the disease disappear more quickly, but the reactions were practically *nil*, and no toxic phenomena occurred. As with the last described vaccine, no negative phase was produced; we have also had good results with a vaccine sensitized with fluid obtained from a gonococcal joint which we had demonstrated to be fairly rich in antibody.

## THE SUPERIORITY OF GONOCOCCAL VACCINE SENSITIZED WITH HUMAN IMMUNE SERUM OVER THAT SENSITIZED WITH IMMUNE HORSE SERUM.

The causes of this marked difference seem to us to be as follows: The gonococcal emulsion contains probably two constituents: (a) the killed bacteria themselves; (b) endotoxins liberated from them.

To produce a completely sensitized vaccine, which will not exert any deleterious effects, it is necessary to employ an immune serum which will combine with or neutralize both (a) and (b)—in other words, the immune serum should contain both a bactericidal substance and an "anti-endotoxin." Now we know from our experiments that the immune horse serum did undoubtedly contain some specific antibody which gave a strong complement-fixation test, but since toxic symptoms followed its use it may be inferred that the immune horse serum contains, on the other hand, no anti-endotoxins. These soluble products remaining uncombined cause the ill-effects which are so constant after the administration of the subcutaneous and intravenous injections of ordinary vaccine. The human immune serum, on the other hand, contains all the antagonistic substances elaborated in the course of the natural disease. These will include both bactericidal substances and anti-endotoxin, since the micro-organisms are living and multiplying in the body, while at the same time some of them are continually being destroyed and setting free their endotoxins.

We employed our sensitized vaccines by giving doses of 20, 50, and 100 million on three successive days; in some cases it appears that one trio is sufficient to cure the case, but in the majority the symptoms ultimately recur, and as the complement-fixation test becomes less positive about the third week, it is wiser to repeat a trio of 200, 300 and 500 million between the second and third week.

We tested the fluid obtained from a joint on three occasions. In every instance it was sterile, no antigen could be demonstrated, but all gave a positive complement-fixation test; in two the reaction was as positive in the knee-joint fluid as it was in the blood. We also used the fluid obtained for therapeutic purposes, but no improvement followed when subcutaneous injections were given around an infected joint.

In conclusion, we would like to warn you to be careful in your selection of an immune serum for sensitizing purposes, since sera vary according to how much antibody they can anchor on to the antigen; therefore a vaccine should not be passed as sensitized unless the serum used for the process has become robbed of its antibody, which can be estimated by the complement-fixation test.

CHART I.—CASE OF GONOCOCCAL ARTHRITIS TREATED WITH ORDINARY VACCINE.

*Complement-fixation Tests.*

|  |     |     |     |     |     |   |   |   |
|--|-----|-----|-----|-----|-----|---|---|---|
| Day of first injection                           | ... | ... | ... | ... | ... | + | + | + |
| Forty-eight hours after injection                | ... | ... | ... | ... | ... | - |   |   |
| Day of second injection (eight days after first) | ... | ... | ... | ... | ... | + | + | + |
| Forty-eight hours after injection                | ... | ... | ... | ... | ... | + |   |   |
| Day of third injection (eight days after second) | ... | ... | ... | ... | ... | + | + | + |
| Forty-eight hours after injection                | ... | ... | ... | ... | ... | + | + | + |
| Day of fourth injection (two weeks after third)  | ... | ... | ... | ... | ... | - | + |   |
| Forty-eight hours after injection                | ... | ... | ... | ... | ... | + | + | + |
| Day of fifth injection (eight days after fourth) | ... | ... | ... | ... | ... | + |   |   |
| Forty-eight hours after injection                | ... | ... | ... | ... | ... | + | + | + |

CHART II.—CASE OF GONOCOCCAL ARTHRITIS TREATED WITH INTRAVENOUS INJECTIONS OF AN AUTOLYSED VACCINE.

*Complement-fixation Tests.*

|   |     |     |     |     |     |   |   |   |
|---|-----|-----|-----|-----|-----|---|---|---|
| Before first injection                            | ... | ... | ... | ... | ... | + | + |   |
| Forty-eight hours after first injection           | ... | ... | ... | ... | ... | + | + |   |
| Five days after first injection                   | ... | ... | ... | ... | ... | + |   |   |
| Day of second injection (six days after first)    | ... | ... | ... | ... | ... | + |   |   |
| Forty-eight hours after second injection          | ... | ... | ... | ... | ... | + | - |   |
| Day of third injection (ten days after second)    | ... | ... | ... | ... | ... | + |   |   |
| Forty-eight hours after third injection           | ... | ... | ... | ... | ... | + | - |   |
| Day of fourth injection (seven days after third)  | ... | ... | ... | ... | ... | + | + |   |
| Forty-eight hours after fourth injection          | ... | ... | ... | ... | ... | + | + |   |
| Day of fifth injection (seven days after fourth)  | ... | ... | ... | ... | ... | + | + | + |
| Forty-eight hours after fifth injection           | ... | ... | ... | ... | ... | + | + | + |
| Day of sixth injection (seven days after fifth)   | ... | ... | ... | ... | ... | + | - |   |
| Forty-eight hours after sixth injection           | ... | ... | ... | ... | ... | + | + | + |
| Day of seventh injection (eight days after sixth) | ... | ... | ... | ... | ... | + | + |   |
| Forty-eight hours after seventh injection         | ... | ... | ... | ... | ... | + |   |   |
| Ninth day after eighth injection                  | ... | ... | ... | ... | ... | + |   |   |
| Three weeks                                       | ..  | ..  | ..  | ..  | ..  | - |   |   |

CHART III.—CASE OF GONOCOCCAL PROSTATO-URETHRITIS AND EPIDIDYMITIS, TREATED WITH VACCINE SENSITIZED WITH ANTIGONOCOCCAL SERUM OBTAINED FROM A HORSE.

*Complement-fixation Tests.*

|                                |     |     |     |     |     |   |   |   |
|--------------------------------|-----|-----|-----|-----|-----|---|---|---|
| Day of sensitized vaccine, 20° | ... | ... | ... | ... | ... | + |   |   |
| " " 50°                        | ... | ... | ... | ... | ... | + | - |   |
| " " 100°                       | ... | ... | ... | ... | ... | - |   |   |
| Three days after trio          | ... | ... | ... | ... | ... | + | + | + |
| Eight " " "                    | ... | ... | ... | ... | ... | + | + | + |
| Ten " " "                      | ... | ... | ... | ... | ... | + | + | + |
| Seventeen days after trio      | ... | ... | ... | ... | ... | + |   |   |
| Twenty-one days " "            | ... | ... | ... | ... | ... | + |   |   |
| One month " "                  | ... | ... | ... | ... | ... | + | - |   |
| Five weeks " "                 | ..  | ..  | ..  | ..  | ..  | - |   |   |

### Further Studies in Experimental Fever.

By E. C. HORT and W. J. PENFOLD.<sup>1</sup>

WE have recently shown that in the experimental study of fever there are numerous sources of error previously undescribed. Some of these pitfalls are fairly obvious and easy to explain—after one has plumbed their depths, as we have done with unfailing precision. Others there are which at present are not easy to understand, though they are on that account none the less definite. The following two sources of error are very difficult to explain, and as we have fully dealt with them elsewhere they need not be more than named.

(1) The first is due to the fact that the degree and duration of the fever produced by injection of constant quantities of a given pyrogenetic agent depends to a considerable extent on the volume of the diluent or suspending fluid employed.

(2) The second is due to the fact that the extent of fever which may follow the injection of constant quantities of pyrogen in constant quantities of pure normal saline (relatively to body-weight) is much more irregular than is the extent of fever which may follow injection of the same quantities of the same pyrogen in the same quantities of pure water.

A third fallacy which proceeds from the use, as a medium of injection, of water or saline that has become contaminated with the heat-stable filter-passing pyrogen we described last year, is somewhat easier to explain, though the source and nature of this elusive body are still quite unknown. Its unsuspected presence seriously impairs, however, as we have shown, the value of the experimental evidence hitherto relied on in favour of various types of injection fever. At the present moment such distinct entities of fever as water fever, salt fever, salvarsan fever, lactose fever, glucose fever, saccharose fever, protein fever, nuclein fever, tissue fever, fibrin ferment fever, serum fever, blood cell fever, hæmolytic fever and anaphylactic fever stand on no sound experimental basis. We have taken each of these one by one and have so far been unable to demonstrate their existence if pyrogen-free water or saline be employed as the

<sup>1</sup> From the Lister Institute. (This paper was read at the Laboratory Meeting of the Section at the Lister Institute on November 5, 1912.)



injection medium. To this list we are now able to add transfusion fever in the sense of the fever which may follow the injection of defibrinated blood and which Freund describes as amboceptor fever. In the experiments quoted by Schultz and Freund in favour of this transfusion fever no controls were quoted to show (a) that infection of the blood had not taken place *in vitro*, (b) that if the blood were diluted the diluent employed was pyrogen-free. We have carried out both these controls, as Chart I will show, and we find that we cannot get fever in rabbits by intravenous injection of defibrinated blood if it is free from laboratory infection or if it has been diluted with pyrogen-free water.

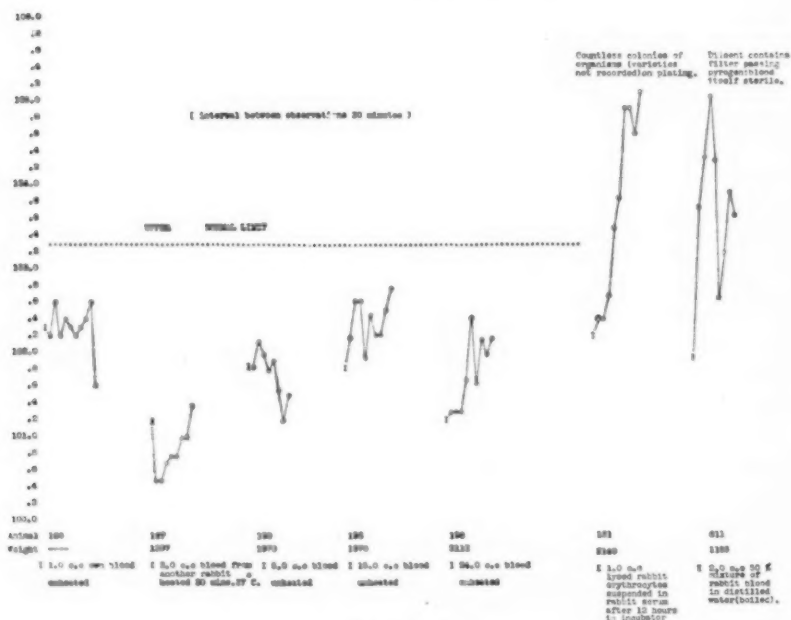
In the experiments we are about to describe these fallacies are avoided by using constant volumes of pure water as our injection medium.

#### CHART I.

##### *Sterile Defibrinated Blood does not produce Immediate Fever.*

Full recognition of these three sources of error is, we believe, of the first importance in the study of experimental fever. To these may possibly be added a fourth, as we showed in December of last year, and, more fully, in July of this year. We refer to it again now on account of further experiments we have carried out since July, 1912. These experiments are by no means completed, and we only bring them forward now in the hope of eliciting criticism, and, if we can get them, suggestions. This fourth fallacy, if it be a fallacy, affects the study of the fever that sometimes follows the injection in pure water or saline of laboratory-grown organisms in the dead or living state. We have already produced evidence, of a somewhat circumstantial nature, that the early fever which alone follows the injection into rabbits of certain types of living or dead organisms that have been grown on artificial media is due not to bacterial pyrogen but to a pyrogen liberated from the medium by the action of the living organisms on that medium. We also showed that certain strains of certain other types of organisms did not when injected alive or dead produce early fever, but did, if injected alive, produce late fever. We therefore grouped in a purely provisional manner the different kinds of organisms we examined according to whether they did or did not, on intravenous injection into rabbits, produce an early fever. This early fever is of short duration, has no latent period, and shows a rapid rise and a rapid fall. The fever is in every

respect exactly similar to that produced by injection of water pyrogen, which, as we have repeatedly found, may bear no relation to the number of organisms capable of cultivation from the water containing it immediately prior to sterilization. On the other hand, it is quite unlike any known form of continued fever occurring in man or animals in the course of a natural infection. This is no doubt partly due to the absence of the continuous supply of pyrogen that obtains in a natural



### CHART I.

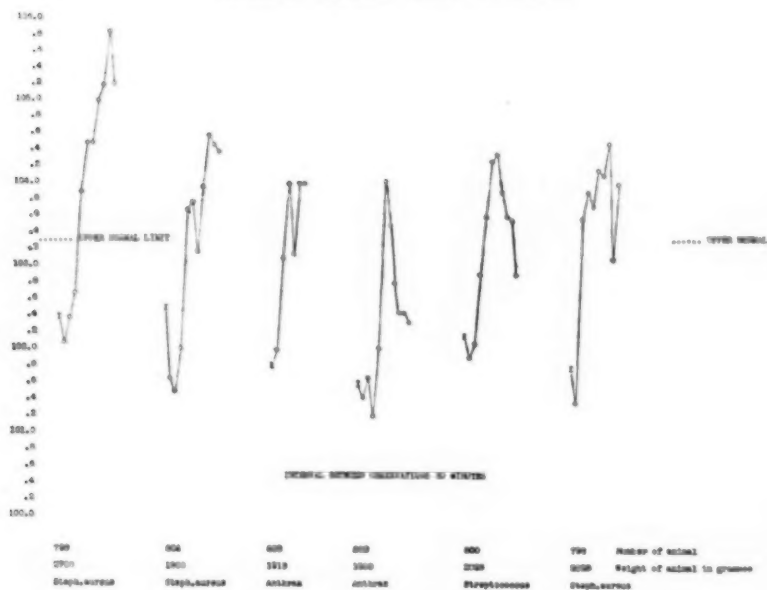
infection. On the other hand, we have as yet been unable to produce a late continuous fever in rabbits by injecting organisms in this group, no doubt on account of the insusceptibility of this animal to infection with some members of this group. Organisms, however, in the second group show, as regards certain strains, a marked contrast. Certain strains, for example, of the types of organisms that, living or dead, caused no early fever produced a late fever in the case of the living organism. This late fever has a well-marked latent period, as its name implies, a gradual rise, sometimes maintained,<sup>9</sup> for many

days, and in cases of recovery a gradual or rapid fall. This fever was in no case fugitive, unless the animal died from an overdose, and showed all the classical features of a typical infection fever occurring naturally. Group I was well represented by *Bacillus typhosus* or *Bacillus coli*, Group II by certain strains of *Staphylococcus aureus* or of pneumococcus. In all cases the organisms were grown on the ordinary laboratory media.

Pursuing this subject still further, we now find that members of the first group, for example, *Bacillus typhosus*, preserve to a large extent the immediate pyrogenetic properties we have described in spite of age (within limits of months). We also find that certain strains of various types of organisms in Group II exhibit apyrogenetic properties (as regards early fever) both in old cultures and in young cultures of strains which had not recently passed through the animal body. On the other hand, we find that other strains of the same organisms exhibit powers of producing immediate fever in the case of young cultures but not of old. The bearing of this observation on the preparation of vaccines for therapeutic or protective purposes is, we think, worth further study. Finally we note that there are yet other strains of *Staphylococcus aureus*, for example, which produce immediate fever in the case of young cultures and of old, behaving, in fact, in this respect like *Bacillus typhosus* or *Bacillus coli*. The explanation of these differences is not yet available. It is not, we believe, a question of differences in numerical values, so far as we can tell by such quantitative experiments as we have been able to carry out. We have, on the other hand, some reason for thinking that highly important factors are the original source of the organism and the time relation of passage (followed by fresh cultivation) to injection. We have never yet failed with any strain of *Staphylococcus aureus* to obtain immediate fever if cultivation in the laboratory has been immediately preceded by passage. We require, however, much further study on all these points. In the meantime we show in Charts II and III the respective pyrogenetic powers (as regards early fever) of different strains of organisms in Group I.

### CHART II.

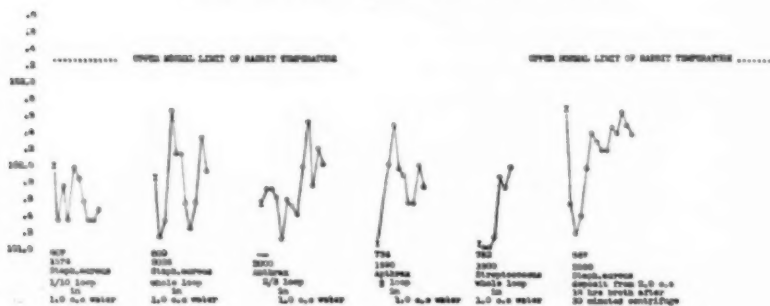
*Certain Strains of Organisms in Group II produce Immediate Fever, whether injected Alive or Dead.*



### CHART II.

### CHART III.

*Certain Strains of Organisms in Group II produce no Immediate Fever whether injected Alive or Dead.*



### CHART III.

In further contrast to the power that certain laboratory-grown organisms have of producing immediate fever in rabbits, we show in Chart IV the effect of injection of organisms after animal passage. At first sight it appears that this chart might be explained on quantitative grounds. It is true that owing to the difficulty of recovering organisms during passage free from salts and other substances derived from the tissues we have not been so far able to devise any satisfactory method of enumeration. Precaution, however, was in all cases taken to obtain positive evidence by films that large numbers were injected. Precaution was also taken by subsequent control cultivation to demonstrate the presence of living organisms. Unless copious growth was obtained the experiments were rejected. We cannot, however, yet claim that we have positively eliminated this source of error. It is conceivable that the absence of fever is due to exhaustion of pyrogen *in vivo*, as most of the animals were suffering from fever when the organisms were recovered. We have, however, guarded ourselves against this source of error to some extent by recovering the organisms in early stages of the fever as well as in late, and by injecting as large numbers of organisms as we could secure. In all the cases shown, as well as in numerous others not charted, we have not yet been able to produce early fever whatever the stage of infection, by injecting washed organisms after passage in the living or dead state, so long as laboratory cultivation was not subsequently employed. This is true even of considerable quantities of pus recovered from young abscesses and injected at once. In some of these cases the presence of a sufficient number of virulent organisms to produce late fever, rapidly followed by death in thirty-six to forty-eight hours after injection, was clearly shown. The experiments shown in this chart strongly recall the experiments we published last year, in which we showed that we could produce no fever by injecting large numbers of dead organisms found in saline exposed to the air, provided that they were injected in pyrogen-free water. They also recall the experiments we quoted in July, in which we found that we could not produce fever by exposing defibrinated blood to aerial infection provided we injected the killed organisms, the living organisms producing marked early fever, perhaps owing to obliteration of latent period. The contrast between these experiments and the results of injecting certain organisms from nutrient media exposed to aerial infection we have already shown elsewhere. We wish, however, to repeat that further work is still required on all these points.

## CHART IV.

*No Immediate Fever follows Injection of Organisms after Passage.*

When we turn, however, to organisms recovered after passage and then cultivated in the laboratory we find that organisms that previous to passage produced little or no immediate fever, and during passage

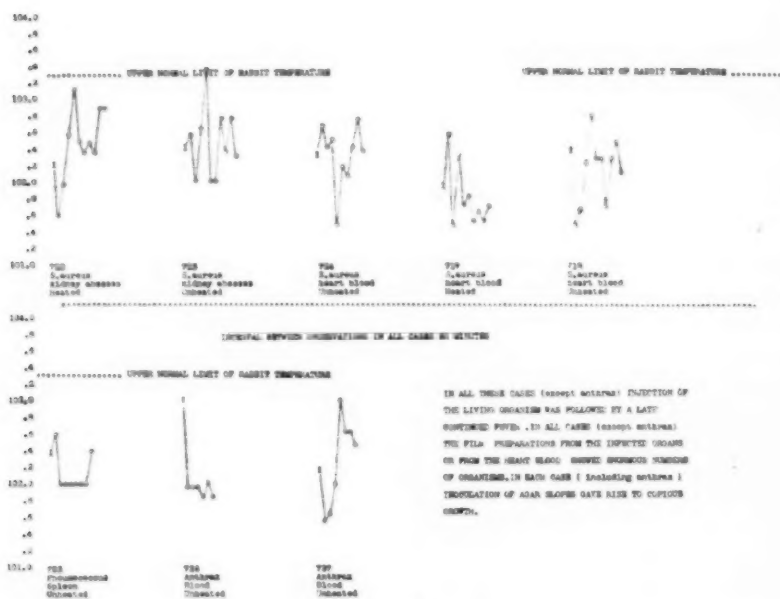


CHART IV.

had the same negative effect, now produce immediate fever. We see, for example, in Chart V that a certain strain of pneumococcus produced on injection no early fever. In two days after injection a continued fever set in. On the eighth day, the fever still continuing, the animal was killed. A large loopful of splenic pulp stuffed with organisms obtained under careful aseptic conditions was injected into a healthy rabbit and no immediate fever followed, but the animal died in three days. At the moment of injection an agar slope was inoculated with a fragment of splenic pulp, and by the next morning a copious growth

was obtained. A measured quantity equal to that first injected was given to a third animal and immediate fever resulted. This animal also died. The same experiment was repeated with a subvirulent strain of anthrax, and also with a streptococcus and several strains of *Staphylococcus aureus*, recovered either from the heart blood or from kidney abscesses. An important point not shown on the chart is the fact that the immediate fever was produced by the dead organisms as well as by the living in several cases of *Staphylococcus aureus* (the only type so far tested as regards killed organisms). If this proves to be generally true, it suggests that passage plus cultivation confers on an organism not only increase of virulence demonstrable *in vivo*, but also a power with which such organism was not previously endowed, of liberating from an artificial medium a pyrogenetic substance. In other words, passage plus cultivation possibly selects from an organism that has not the power of producing immediate fever, alive or dead a strain that has that power alive and dead. We prefer, however, at present not to do more than indicate the possibilities involved in this branch of work, as further experiment is required on the effect of subcultivation without passage. If further study confirms our suspicion that the more or less immediate toxic effects quâ fever, so often seen in man after injection of dead vaccines, are partly due to contamination of such vaccines with pyrogen derived from the laboratory media, this is an accident that it may become necessary to prevent. We have already shown that living and dead *Bacillus typhosus* vaccines, for example, can be readily detoxicated, as regards immediate fever, in the test-tube by mere keeping or by oxidation, and we are now studying the relative antigenic values, in terms of test-tube reactions, of ordinary vaccines and of detoxicated vaccines. In the meanwhile we are content to submit that, in the light of our observations, the fact that certain organisms after culture in the laboratory are capable of producing immediate fever when injected dead cannot be taken as good evidence as to the source of the supply of pyrogen in infective disease.



CHART V.

*The Apparent Effect on Pyrogenetic Function of Passage plus Cultivation in the Laboratory.*

(Compare with Chart IV.)

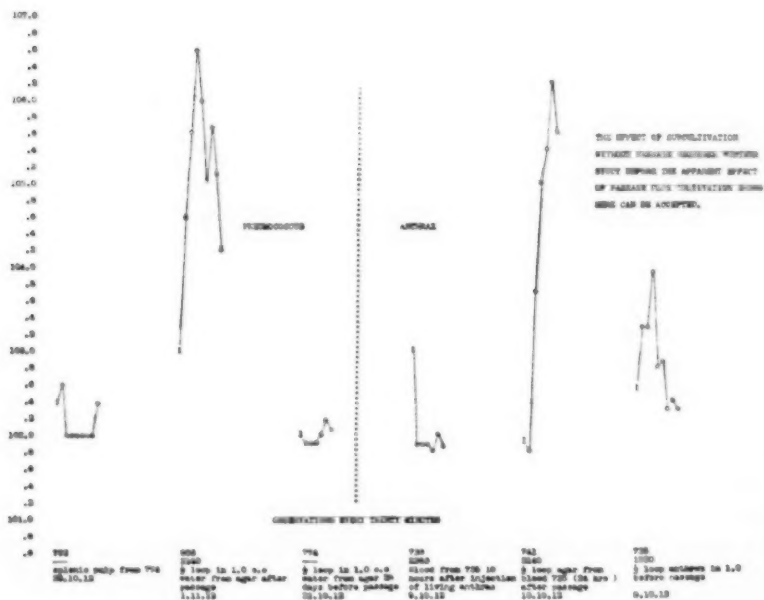


CHART V.

## Pathological Section.

December 3, 1912.<sup>1</sup>

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### The Complete Life-history of the Organism of Syphilis.

By J. E. R. McDONAGH, F.R.C.S.

THE sporozoite when examined *in vivo* remains for some time unstained, but later stains very deeply without its motility becoming thereby impaired. It is seen in two forms—(a) circular, (b) renal-shaped—its size is about  $1\frac{1}{2}$  microns in diameter, and it is actively motile; occasionally I have seen distinct flagellæ attached to it. Besides being found in the scrapings from syphilitic lesions, it can be found in the blood withdrawn from the healthy skin surrounding a chancre and also in the general blood-stream during the stage of general infection. I have found it in the former when I was unable to find the *Spirochæta pallida* in the scraping from the sore; therefore the sporozoite is of great diagnostic importance. The sporozoite then becomes intracellular. On two occasions I have seen it in a small mononuclear leucocyte: it remained actively motile while within and ultimately left the cell. The cell it makes its host is a connective tissue cell, and when inside it undergoes important changes, which can best be described under two headings:—

(1) The sporozoite steadily increases in size, and by a process of budding gives rise to several bodies which later become differentiated into male and female elements. By this time the cell is a sac, as all the reserve material has been used up by the merozoites, but the nucleus still remains although degenerated, and then it finally disappears when the sac gives way and frees the male and female merozoites. Not all the bodies formed in this way are sexually differentiated; there are others which become free with the sexual merozoites and are able to start the cycle again by seeking a fresh connective tissue cell.

<sup>1</sup> Laboratory Meeting held at the National Hospital, Queen Square, W.C.

(2) The sporozoite increases in size, but not to the dimensions met with in the previous case. Having reached a certain size, it divides into two, and again into four; after the primary division the karyosome

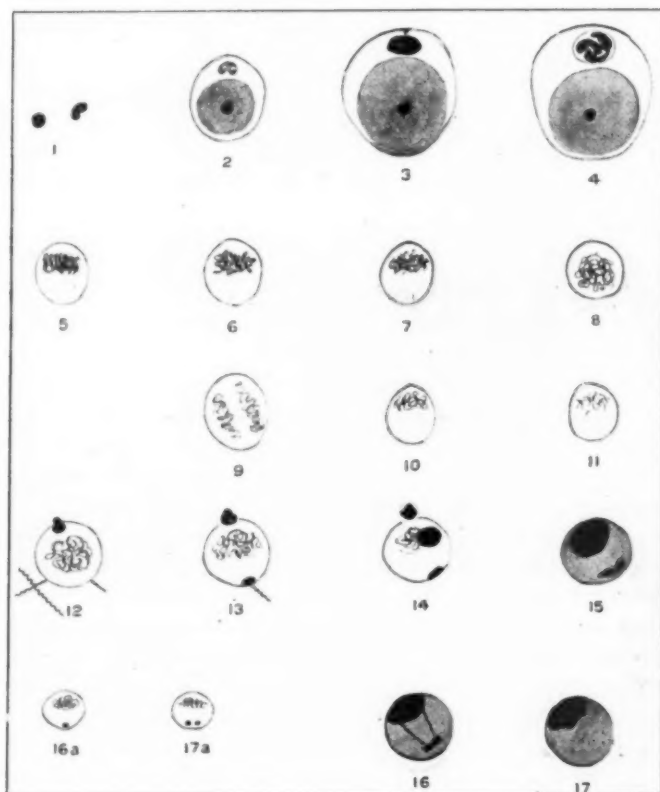


FIG. 1.

Bodies seen *in vivo* stained with borax methylene blue. 1, sporozoites; 2, sporozoite in small mononuclear; 3, male gametocyte in large mononuclear; 4, three pear-shaped bodies; 5, 6, 7, female gametocytes; 8, female gamete; 9, 10, 11, parthenogenesis; 12-17, fertilization and zygote-formation; 16a, 17a, young female gametocytes.

disappears. These four masses, by a process of further subdivision, form a ring and migrate to the periphery of the body, then a picture is given as if the ring had stones mounted in it the whole way round. By this

time the host cell is almost completely degenerated, and one might imagine that the parasite had become extracellular, while it only does so when the host cell is no more. In the centre and around the ring other deeply stained bodies appear, until a picture of a perfect spore cyst is given. This is doubtless the true asexual stage, and the two stages just described represent the schizogony.

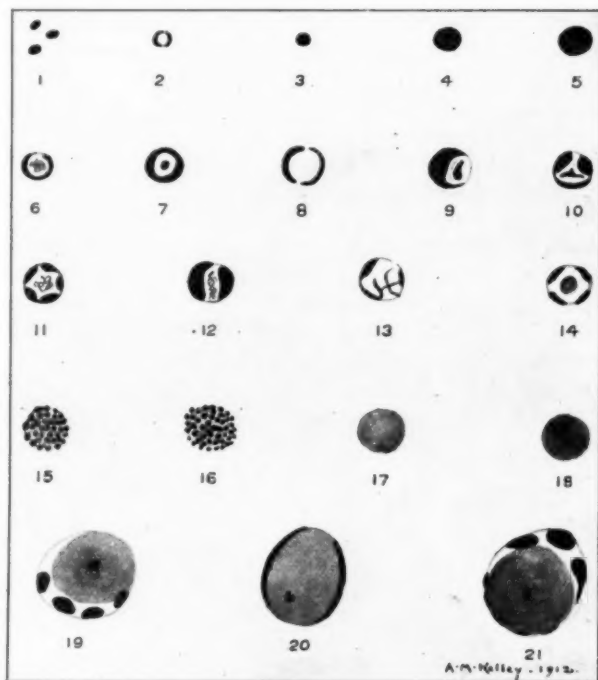


FIG. 2.

Bodies seen *in vivo* stained with borax methylene blue in normal and inflamed glands. 1-14, developing lymphocytes; 15, 16, developing granular leucocytes; 17, 18, red blood corpuscles (note chromatic filaments in 18); 19-21, normal mononuclears.

The sexual generations develop as follows: The male, which is a circular or sometimes oval-shaped body, is actively motile and flagellated. In the course of its progression it approaches a large mononuclear lymphocyte and enters it; it appears to become motionless the moment the cell is reached. Inside the large mononuclear it increases in size and soon loses its karyosome, and then later three pear-shaped bodies are

discernible. The merozoite, as I think it may be called, or the male gametocyte, steadily develops until a coil is formed. In some of the coils deeply stained structures are to be seen; these probably correspond to the pear-shaped bodies above mentioned, and it is also probable that the bodies seen with spirochætæ coming off like the spokes of a wheel from its axle are still further developments of the same structures.

In many specimens stained *in vivo* streptococcus-like chains are numerous, and also many free coccus-like bodies, which come from the former. On careful examination each coccus-like body is found to

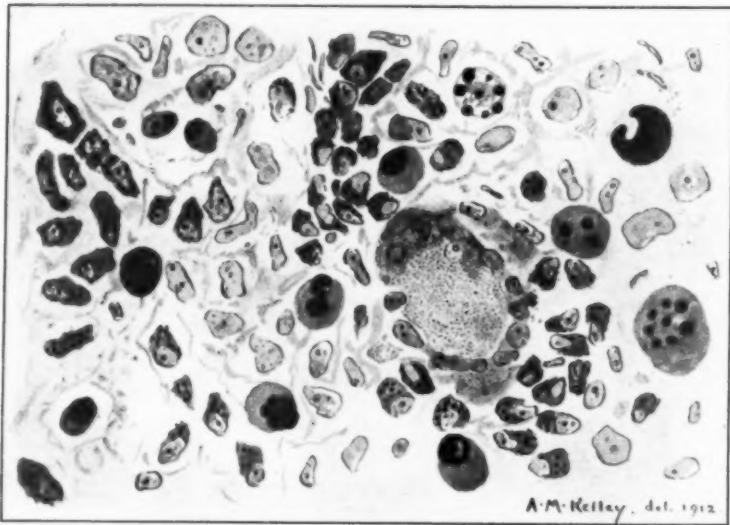


FIG. 3.

Section of syphilitic lymphatic gland stained with pyronin and methyl green.

consist of a clear ring which contains in its interior two deeply staining rods one above the other, so that the impression of a diplococcus is given. These coccus-like bodies are motile, and their form is clearly visible when examined with the dark-ground illumination. I cannot be certain whether each rod parts company or becomes one, but nevertheless they increase in length, and finally develop into spirochætæ. Moolgavkar and I have also demonstrated this development in a culture from a chancre grown in pure ascites fluid anaerobically, and we found that it took more than a fortnight for even the un-

developed spirochætæ to evolve. These coccus-like chains and bodies presumably develop from the coils. Another body which leaves the connective tissue cell is oval or circular, motile, and occasionally appears to be flagellated, but, instead of staining homogeneously, is a clear body containing a faintly stained chromatin network at its upper pole, and one or two deeply stained rods or dots at its lower pole. The future life of this body is extracellular, and it is doubtless the female gametocyte. The gametocyte increases in size until it equals a red

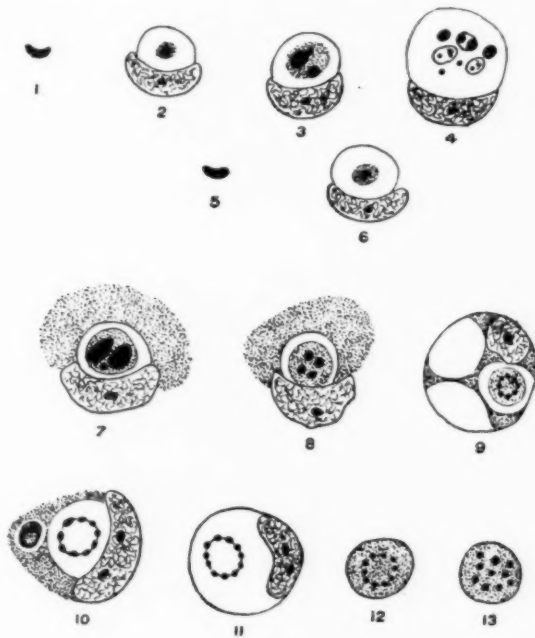


FIG. 4.

Schizogony as seen in sections. 1-4, sporozoite in connective tissue cell becoming sexual merozoites; 5-13, sporozoite in connective tissue cell becoming asexual spore-cyst.

blood corpuscle. In my Giemsa-stained specimens the chromatin network has stained homogeneously, which gives it that crescentic appearance which I described and figured in my last communication. The deeply staining small dot, or dots, as there may be two, at the lower pole of the cell, which are actively motile, are probably the blepharoblasts, which later leave the cell, as in a number of cells no such body

is seen. The chromatin network increases in size until it practically fills the centre of the cell, hence the homogeneous staining of the whole cell as seen in Giemsa preparations. Such a cell is probably the female gamete and ready for fertilization.

The act of fertilization I have been fortunate enough to witness, and it occurred after this style: The female cell to the left of the upper

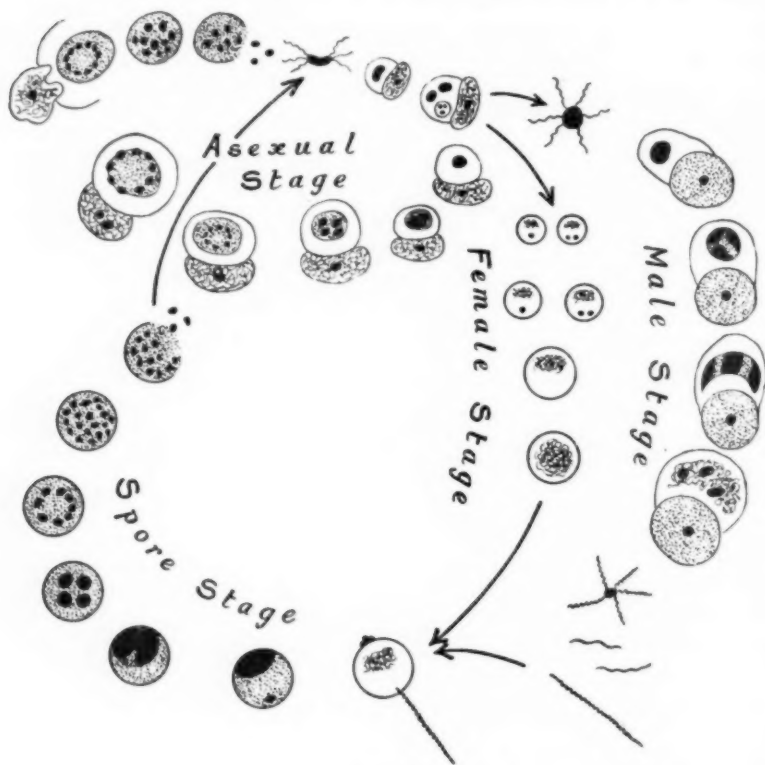


FIG. 5.

Schematic representation of life-cycle of *Leucocytozoon syphilis*.

pole had attached to it a deeply staining body shaped like a cottage loaf; to the right of the lower pole a *Spirochæta pallida* had entered, and close beside lay two more spirochætæ. The whole was in active motion. The two spirochætæ soon disappeared. The cottage-loaf body became



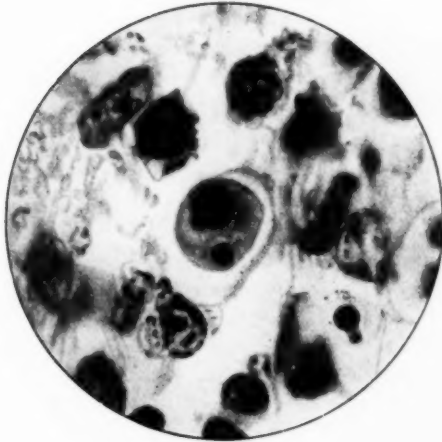


FIG. 6.

Trophozoite dividing into sexual merozoites in a connective tissue cell. ( $\times 1,500$ .)

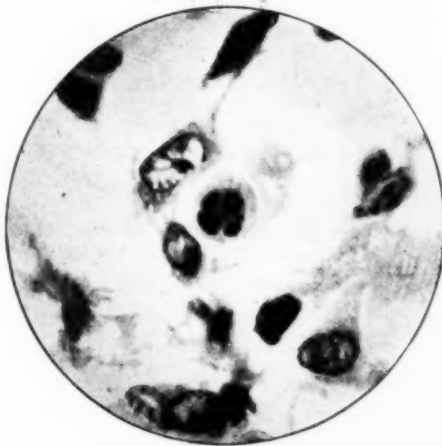


FIG. 7.

First subdivision of trophozoite in development of asexual spore-cyst in a connective tissue cell. ( $\times 1,500$ .)

more and more extracellular, until it was ultimately free. The cottage-loaf body must be the extruded polar body or bodies. The chromatin network became more deeply stained and migrated towards the upper pole, while the spirochæta which had entered became a deeply stained, more or less rod-shaped body at the lower pole. The chromatin network was now entirely at the upper pole and one half of it had become a homogeneous darkly stained mass, and the whole cell took on a rose-pink stain. During the performance the cell suddenly came to a standstill. Examined a little more carefully, I could make out that the male element appeared to divide into two, and became connected with the female by delicate deeply stained strands. These strands then

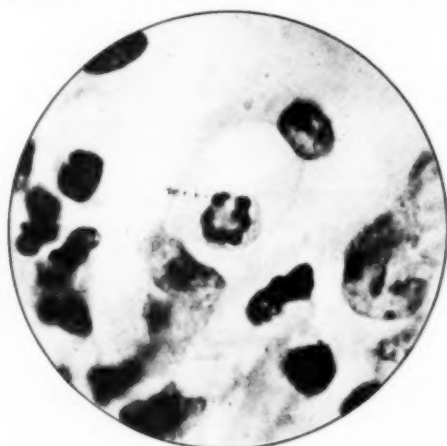


FIG. 8.

Further division of trophozoite in connective tissue cell. ( $\times 1,500$ .)

appeared to contract, and so pull up the male element into the female. In the next stage no male element was visible at all, but in the female were two very deeply stained dots which no doubt represented the former. The whole of the chromatin network finally becomes transformed into a deeply staining mass, one part of which remains attached to the circumference of the cell: such a cell is no doubt the zygote. The fertilized females or zygotes can be distinguished from the gametocytes by the fact that in the former the background of the cell is stained while in the latter it remains clear. Females can possibly multiply by division—parthenogenesis—as I have seen larger oval-shaped bodies with an elongated chromatic network on either side, the networks being quite

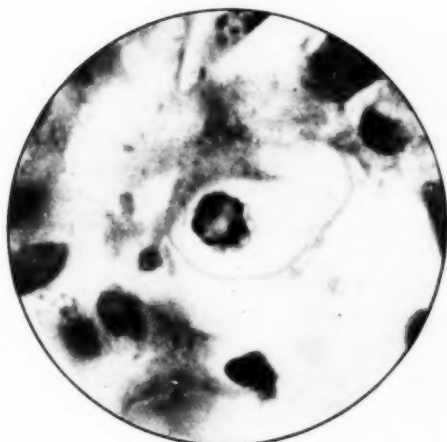


FIG. 9.

Still further division of trophozoite, nearly extracellular. ( $\times 1,500$ .)

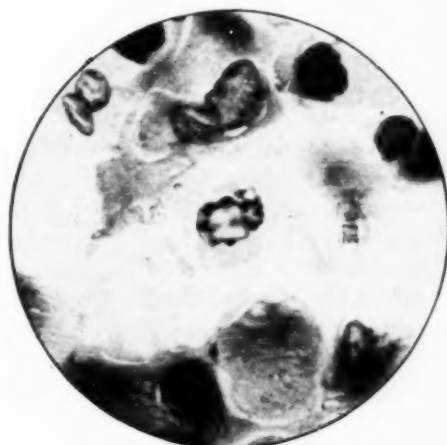


FIG. 10.

Asexual spore-cyst; extracellular. ( $\times 1,500$ .)

distinct from each other. Division then takes place and two female gametocytes are formed. In these bodies no blepharoblasts are to be seen. On the other hand, it is quite probable that the phenomenon so witnessed was mitosis in a plasma cell, as some of the plasma cells *in vivo* resemble female bodies very closely. The changes of the zygote up to the formation of the spore-cyst do not differ in any way from my previous description, and are well portrayed in the illustrations. Occasionally tiny little spore-cysts about 4 microns in diameter are to be seen, which I cannot help thinking develop from escaped sporoblasts from the oökinet.

*Frequency of the Different Bodies.*—In early active syphilitic lesions the sporozoites are seen to best advantage, and in almost every specimen a coil and spore-cyst are to be found. In some of the glands which I have examined I have found practically nothing else but coils, there being sometimes as many as five or more in a field. In most specimens the female gametocytes and zygotes are to be found in greatest abundance; it seems that neither salvarsan nor mercury has any influence upon them, as Price and I have found them in every lymphatic gland we have examined from patients who have had from one to ten injections of salvarsan. They are equally common in cases which have no symptoms as in those that have, and no relationship can be found to exist between their presence and the result of the Wassermann's reaction.

*Traps.*—The examination of lymphatic glands is accompanied by innumerable possible pitfalls to which I would like to draw your special attention: (1) Some dark-staining motile dots are frequently to be seen, but they are smaller than the sporozoites. (2) Circular bodies in all sizes from 1 to 7 microns are invariably to be found in every inflamed gland: they resemble superficially the female gametocytes, but can be distinguished by the fact that they contain no chromatin network, and the darkly staining masses of which they are made up are mostly situated in the circumference of the cell itself, so that one or more of these darkly stained masses are crescentic in shape. From fig. 2 you will notice that there is a close resemblance between the mature lymphocytes and the small circular bodies with the crescentic masses, since in both instances the most deeply stained part of the lymphocyte and tiny body is the periphery, which in the former may be stained in its entirety, or more generally irregularly, with a preference for one pole where deeply staining masses are to be found, which ultimately become extracellular. I think it is highly probable that the small bodies referred to are immature lymphocytes. (3) Endothelial cells which contain circular

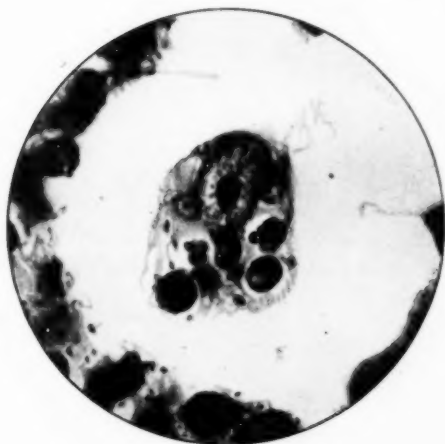


FIG. 11.

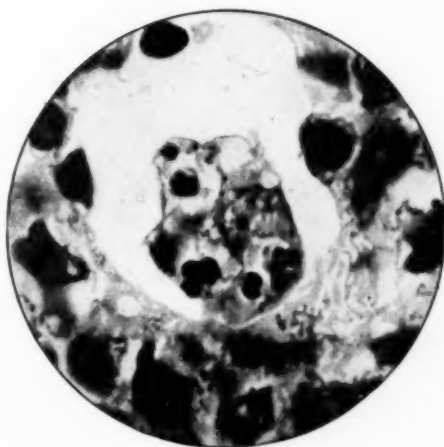


FIG. 12.

Figs. 11 and 12.—Endothelial cells with protoplasmic masses within, which probably become lymphocytes; might be mistaken for schizogony in connective tissue cells. ( $\times 1,500$ .)

masses of varying sizes in their protoplasm; the cell ultimately bursts and these masses escape. It is in Giemsa-stained specimens and in sections that these masses are most likely to be mistaken for the connective tissue syphilitic bodies. In the case of the former no bodies should be taken for parasitic unless they have a background, which in my specimens closely resembles the colour of a red blood corpuscle. In sections the distinction is more apparent. The endothelial masses stain a dazzling transparent red (pyronin) and look as if they had no depth in them; the centre is usually clear, or it would be better to say that the most deeply stained part of the mass is the periphery; furthermore,

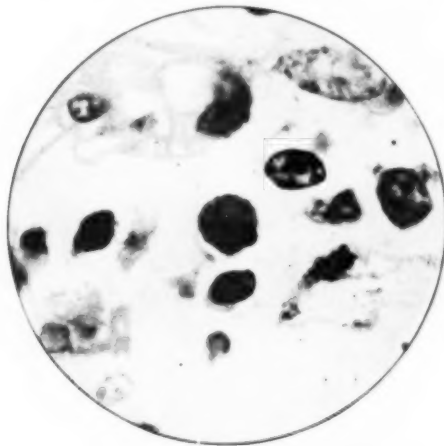


FIG. 13.

Fertilized female zygote. ( $\times 1,500$ .)

some of the masses stain green (methyl green), which is some evidence of their not being parasitic.<sup>1</sup> Far and away the most distinguishing feature is the fact that the syphilitic bodies are massed together in one clear encapsuled space, while the endothelial masses are scattered about anywhere in the cell. The syphilitic bodies, as you will see from fig. 3,<sup>2</sup> have a rose-pink to red background, with their nuclear structure situated more or less at one pole appearing eccentrically placed and very deeply stained, sometimes to a very dark red, or even brown, and most of the syphilitic bodies have a clear space or halo surrounding them. The

<sup>1</sup> Some of the spores in the asexual spore-cyst stain green.

<sup>2</sup> In the original this plate is coloured.

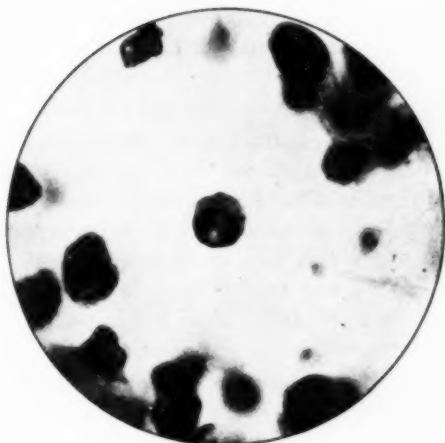


FIG. 14.

Zygote dividing. ( $\times 1,500$ .)

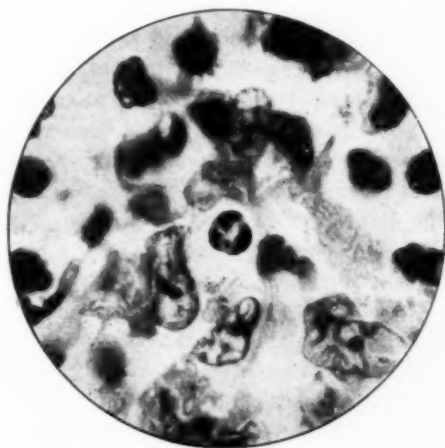


FIG. 15.

Male with three pear-shaped bodies; nucleus of mononuclear scarcely visible. ( $\times 1,500$ .)



similarity in specimens stained *in vivo* between the extracellular parasitic bodies and the plasma cells, and those red blood corpuscles which contain some chromatin filaments, should complete the enumeration of the difficulties.

The non-syphilitic bodies above described are found in every inflamed lymphatic gland, even in syphilitic glands; therefore, those of you who intend to study this subject should first examine normal glands and glands enlarged from diseases other than syphilis. The method I have used for staining *in vivo*—viz., with borax methylene blue—is carried out as follows: A film of Grüber's borax methylene blue should be made and allowed to dry on a fat-free slide; the scraping to be examined should be placed upon a cover-slip, which should be inverted and pressed down on to the slide, so that no air remains in between; the cover-slip can then be ringed round with wax.

Quite contrary to what might be expected, practically the whole life-history of the syphilitic parasite can be followed out in one section from a lymphatic gland which drains the primary sore, if it is removed during the stage of general infection and stained with pyronin and methyl green; even the spirochaetal coil is discernible. Lately I have tried staining films with Giemsa after they have been fixed while wet in a hot and then a cold alcoholic solution of corrosive sublimate, and further treating the section before staining with Lugol's solution and sodium thiosulphate. This method is no doubt an improvement over the old, but it is laborious, and from a practical point of view cannot come up to the *in vivo* method of staining with borax methylene blue. It must be remembered that quite a different impression is given of these bodies according to how they are stained. From the above description of the life-history of the organism of syphilis, I think I am justified in assigning it to the order Sporozoa and to the sub-class Telosporidia, since the spores are formed at the end of a cycle. The order is doubtless the Coccidiidea, and the species which most befits it is the *Leucocytozoon*; hence a good name for the syphilitic parasite would be *Leucocytozoon syphilis*.

In conclusion, I would like to mention that I have found bodies stained *in vivo* in the lymphatic glands of rats which have died from an infection caused by *Trypanosoma rhodesiense*, which are indistinguishable from the syphilitic macrogametocytes and zygotes, and I have also seen the impregnation of the former by the microgamete, and the details of fertilization fit in exactly with those described as occurring in syphilis.

## Pathological Section.

January 21, 1913.

Dr. R. T. HEWLETT, President of the Section, in the Chair.

### A Preliminary Communication on the Pathogenicity and Virulence of Bacteria.

By F. H. THIELE and DENNIS EMBLETON.<sup>1</sup>

As much of the work on which this paper is based has not yet been published, it is necessary to briefly review the work in order to bring out the argument clearly. First, then, we must consider the mechanism of *fever production*. Friedberger showed that in animals which have been sensitized with serum (for the demonstration of anaphylaxis) a much smaller dose of the protein is necessary for the production of temperature variations than is necessary in unsensitized animals. He also showed that in the early stages after sensitizing an animal a further dose of a protein will produce a rise of temperature, but later on the *same* dose will produce a fall of temperature. Finally, he showed that if anaphylatoxin be prepared *in vitro*, a small dose injected into an animal will produce a rise of temperature, a larger dose a fall. From these observations he concluded that these various effects were due to the formation of anaphylatoxin produced *in vivo* on the one hand and *in vitro* on the other, and that the various effects depended on the amount exhibited. Vaughan and Wheeler have shown that repeated doses of protein or bacteria produce temperature variations; the type of variation depending on the dose and frequency of inoculation. They consider that protein and bacteria contain a preformed toxic molecule. Hort and Penfold have shown that temperature variations occur in animals when these are inoculated with certain bacteria. They consider that the temperature variations are due to a substance they designate pyrogen, which substance is supposed to be liberated from the medium on which the bacteria are grown.

<sup>1</sup> From the Bacteriological Laboratory, University College Hospital Medical School.

We have been able to show that—

(1) Given a sufficiency of ferment in an animal, varying quantities of protein or bacteria will produce, when injected, the following conditions:—

|     |                           |     |  |
|-----|---------------------------|-----|--|
| (a) | A sufficiently small dose | ... | No temperature variation.                      |
| (b) | A larger dose             | ... | A temperature rise.                            |
| (c) | " " still                 | ... | A greater temperature rise.                    |
| (d) | " " "                     | ... | Less temperature rise.                         |
| (e) | " " "                     | ... | No temperature variation.                      |
| (f) | " " "                     | ... | A temperature fall.                            |
| (g) | " " "                     | ... | A greater temperature fall, followed by death. |
| (h) | " " "                     | ... | Acute death, so-called anaphylaxis.            |

If, however, there is insufficient ferment present to start with, acute anaphylaxis can never be produced, and so on.

(2) Proteolytic degradation bodies, so-called anaphylatoxin, manufactured *in vitro* produce effects parallel to the above according to the dose.

(3) That by producing varying stages of anti-anaphylaxis (that is to say, the condition following the anaphylactic shock in which recovery has taken place) the conditions following a further dose depend on the amount of ferment used up by the first dose. Friedberger came to similar conclusions from his work. For example, if all the ferment is used up by the first dose, the second dose produces no temperature variation. If most of the ferment is used up, the second dose produces a temperature rise. If little ferment is used up, the second dose produces a temperature fall.

(4) By inoculating the tissues of animals sensitized to protein or bacteria into a normal animal, that these passively sensitized animals acquire the power of developing temperature variations after injection of the specific protein.

And we were able to show that if the amount of ferment—i.e., the sensitized tissue injected—was kept constant, temperature manifestations varied inversely with the amount of the protein subsequently injected, and by keeping the protein constant and the ferment variable, similar results were obtained. Also, if normal tissues of animals were injected into normal animals, these animals developed the power of giving temperature variations with smaller doses of any protein than normal animals, this power being due to an increase in the normal ferments, specific or non-specific.

From these observations we have been able to deduce that:—

(1) Temperature variations are due to the interaction of the substance injected and the ferments present, normal or induced.

(2) That the substance which gives rise to the temperature variations is an early degradation product of proteolytic disintegration of the injected substance.

(3) That the rise and fall are both due to the same substance and not different stages of degradation of this substance, but to its rate of accumulation.

The substance in large amounts produces a fall in temperature, in small amounts a rise. So that the results depend on the relative

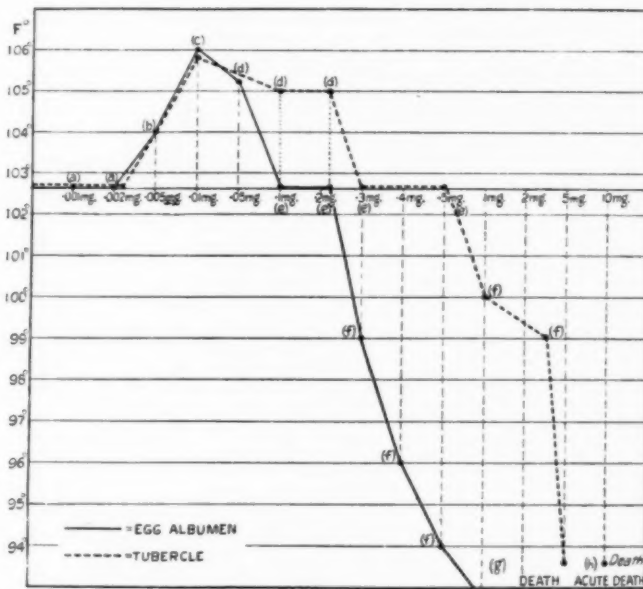


CHART I.

Curves showing maximum temperature variations in animals having the same amount of ferment. The black line shows a series of 14 animals that received the sensitizing dose of egg albumen twenty-eight days previously. The reacting doses are expressed along the 102.6° F. line in milligrammes. The dotted line shows a series of 12 animals that received the sensitizing dose of pulverized tubercle bacilli twenty-eight days previously.

amounts of substance injected and ferment present. If, then, there is sufficient ferment present, any stage can be produced from a single dose, according to its size, from a temperature-raising effect, through a temperature-depressing, through so-called anaphylaxis, to the acute Auer-Lewis phenomenon or acute anaphylaxis.

Hort and Penfold have shown that minimal quantities of certain bacterial broth cultures—for example, *Bacillus typhosus*—when inoculated into normal animals in sub-lethal doses vary in their result according to the degrees of dilution of the culture; that the maximum toxic effect is produced with distilled water, but that the results are inconstant with normal saline. Thus by diluting sub-lethal doses of typhoid broth with distilled water they are able to produce great temperature variations and death.

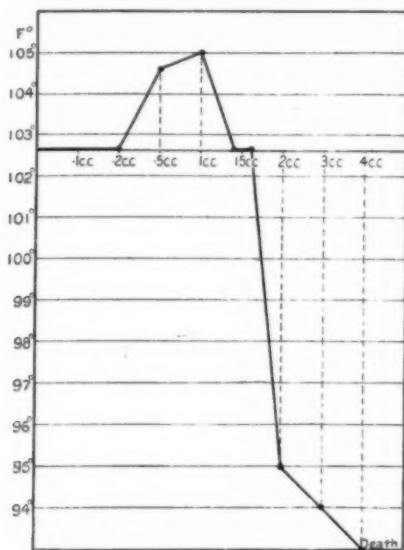


CHART II.

Anaphylatoxin produced *in vitro*. Anaphylatoxin expressed in cubic centimetres of crude toxic serum, along the 102.6° F. normal guinea-pig temperature line.

We have been able to show that the phenomenon of Hort and Penfold can be produced in animals in which the inoculated substance cannot possibly have any preformed pyrogenetic substances, such as sterile egg albumen and sterile washed red corpuscles. We have done this by inoculating guinea-pigs sensitized to the above substances with the homologous antigens in various stages of dilution, in sterile pyrogen-free distilled water, the antigen being in such quantities that undiluted it gave rise to slight or no temperature variations. (These effects can be seen on Chart III.) We imagine that the explanation of this

phenomenon is that, firstly, the ferments are greatly diluted; secondly, that their activity is greatly inhibited by the hypotonicity of the solution; thirdly, that the hypotonicity of the solution renders it more rapidly absorbable, so that the degradation bodies formed are absorbed before they are rendered non-toxic.

The toxicity of a bacterium not possessing an exotoxin was formerly considered to be wholly due to the liberation of an endotoxin. Friedberger considers that toxicity is due to the formation of anaphylatoxin

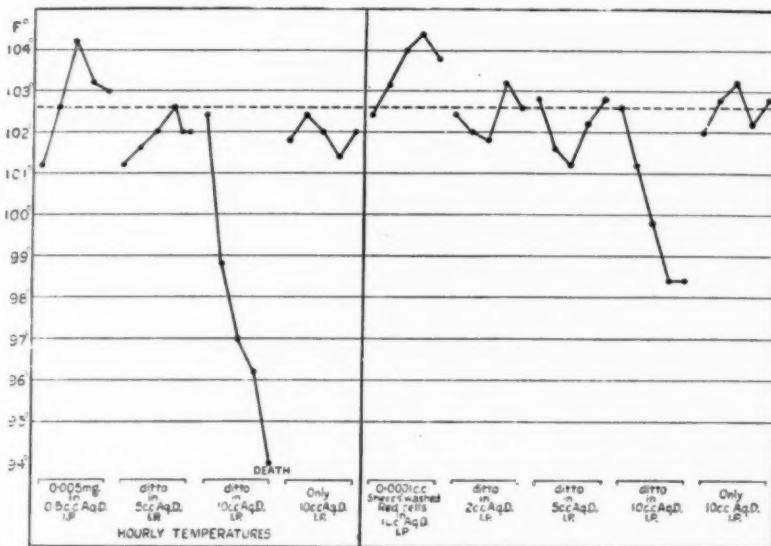


CHART III.

A series of guinea-pigs sensitized with 0.02 gm. of egg albumen one month previously.

A series of guinea-pigs sensitized with 0.06 c.c. of sheep's washed red cells three weeks previously.

from the endotoxin, but does not absolutely deny the possibility of the endotoxin being directly toxic. Now the views held at present with regard to the endotoxin are that it is—

(1) A toxic substance secreted in the animal body.

(2) A preformed toxic molecule which is liberated by breaking up of the bacterial cell: (a) in the animal body by antibodies; (b) *in vitro* by alcoholic potash; (c) *in vitro* by watery potash; (d) *in vitro* by freezing and thawing or by freezing and grinding.

We have been able to show that the so-called endotoxin is really the toxic proteolytic degradation bodies liberated from the bacterial protoplasm by the action of the tissue ferments, and that accumulation of this body in bacterial infection is the cause of the symptoms and death, and is the same for all bacteria; and that this is the same substance obtained by Friedberger *in vitro* or from the peritoneal cavity, using the peritoneal cavity as a test-tube. We conceive that the toxicity of a bacterium depends upon:—

(1) The ease with which its protoplasm is accessible to ferment action.

(2) The nature and amount of ferment present.

Thus, if a bacterium is fragile, the ferments present can attack the protoplasm easily, the toxic substance is liberated readily, and the symptoms depend on the amount of accumulated toxin at any given moment. On the other hand, if the bacterium is tough—for example, the tubercle bacillus with its fatty capsule—the ferments can only act on it very slowly, and consequently the rate of production of toxin is very much slower. Again, within limits, an increase in the ferment will increase the rate of liberation of toxic material from the bacterial protoplasm.

It is said that an animal dying of any form of bacterial infection is supposed to die from the specific poison—i.e., the endotoxin. Now we have been able to show that the blood of these animals contains an intensely toxic substance, which when inoculated into guinea-pigs intravenously, in doses of from 5 c.c. to 10 c.c. produces acute death with the typical symptoms and post-mortem appearances of proteolytic degradation body poisoning. We have obtained this syndrome with the blood of rabbits dying from chicken cholera, coli, Danysz, dysentery, and phlei, and the blood of guinea-pigs dying from staphylococcus, tubercle, proteus, and prodigiosus. We have also produced the same syndrome with the blood of animals which have died of toxæmia from the above-mentioned dead bacteria.

The number of bacteria inoculated with the blood of these animals is extremely small, and is quite insufficient in itself to cause acute death of the type mentioned. In fact, we have shown that when bacteria are completely broken up by freezing and thawing or by grinding, so as to liberate the "endotoxin," death of this description only rarely occurs, and then with quantities of over 20 mg. dry weight. We have succeeded in producing acute anaphylactic death with tubercle bacillary emulsion (B.E.), coli, and proteus. With all other organisms with large quantities, intravenous injection causes delayed death (delayed ana-



phylaxis). The animal develops rigors, ruffling of the coat, fall of temperature below 94° F., paresis spreading from the posterior to the anterior extremities, and disordered respiration. On death, the post-mortem changes are all the same—viz., congestion of the right side and veins, distended gall and urinary bladders, and a certain degree of lung distension. Now these symptoms and post-mortem appearances are identical with those produced by inoculation of egg albumen into egg-sensitized guinea-pigs, in doses too small to cause acute death (or where the ferment is insufficient to cause acute death). Now we have noticed that guinea-pigs dying of any bacterial infection die with these same symptoms and post-mortem appearances. The results obtained by Arima with so-called typhoid toxins—i.e., the soluble and insoluble typhoid protoplasm—are identical with these. Vaughan and Wheeler have produced tissue changes in animals, by the repeated inoculation of egg albumen, which are exactly the same as those produced by bacterial infections. Thus we see that the toxic substance liberated from bacteria in large quantities produces in normal animals symptoms of acute proteolytic degradation body poisoning, in smaller quantities great fall of temperature, paresis, rigors, &c.; in smaller quantities still, fever; and that the so-called endotoxins only give rise to these symptoms when the various ferments have been able to produce the necessary accumulation of degradation bodies to give rise to the symptoms.

In animal infection the difference between the symptoms produced by the different bacteria depend on the distribution, rate of multiplication, and consequent liberation of the degradation bodies. For example, a characteristic clinical picture may be obtained with certain bacteria due to local cumulative effects. In certain structures where the organism is normally present in large quantities and is continually there undergoing proteolytic degradation, for example in the intestines, we always note, in coli infections, intense hyperæmia of the mucous membrane and hyperæmia of Peyer's patches in guinea-pigs. A similar condition was noted by Schittenhelm in dogs, by injection of hydrolytic degradation products of *Bacillus coli*. The acute toxic material of Vaughan and Wheeler, Schittenhelm, &c., are really hydrolytic cleavage products and not unaltered bacterial protoplasm. Friedberger, in his paper on "Anaphylatoxin Fever," drew attention to the similarity between certain features in the syndrome of bacterial infection and those produced by anaphylatoxin.

To summarize:—

(1) Endotoxin as originally understood does not exist. The bacterium does not liberate a primarily toxic substance.

- (2) The bacterial protoplasm itself is not directly toxic.
- (3) The bacterial protoplasm becomes toxic on exposure to ferments.
- (4) The degree of toxicity depends on the accessibility of bacterial protoplasm and concentration of ferment.
- (5) As we shall show later, if the amount of ferment is very large, lysis occurs so rapidly that the bacterial protoplasm is broken down to non-toxic substances.

Now with regard to the ferment and its formation. We have found that working on the early stages of the formation of a hæmolytic antibody in rabbits to human red cells, the development of the specific antibodies can be traced through the following stages from the panenzyme. Complement in its simplest form must be regarded as panenzyme which will attack any form of protein, though slowly. In its earliest stage the specific ferment occurs in such a condition that when exposed to the specific antigen at 0° C. it combines with it, and it is found that the complement, which would otherwise activate sensitized homologous antigen, has been removed, but that the other complements are left free. This ferment is destroyed by heat at 56° C., and cannot be re-activated by the addition of fresh complement. The next stage is the development of a thermolabile amboceptor, which combines at 0° C. and does not fix complement in the cold and by itself will agglutinate. The final stage is the development of the thermostable amboceptor. In the normally occurring hæmolytic antibody (e.g., in rabbits to sheep's red cells) all three stages may be demonstrated to occur at the same time, and it seems that the younger the animal the less differentiated the ferment is. The antibodies to bacteria apparently go through the same stages, but it is only in certain cases that the whole process can be traced. Thus we consider that the complement is an enzyme and the amboceptor is a kinase or co-enzyme which activates and is an adjuvant to the former.

From the above work we thought that organisms were not pathogenic because they produce endotoxin, but were pathogenic to animals because the animals had ferments which were capable of acting on the bacteria so as to cause an accumulation of proteolytic degradation bodies, which would inhibit phagocytosis and allow the bacteria to multiply. With regard to phagocytosis, we shall shortly publish a paper with Dr. Stanley Warren in which it is shown that:—

- (1) Carbon particles and bacteria to which the animal has no ferments act as innocuous substances and are phagocytosed by the polymorphonuclear neutrophils and these in turn by endothelial cells.
- (2) In an animal which is immune from the presence of a large

quantity of ferment the bacteria are very rapidly broken down beyond the toxic stage, and so are innocuous, and the usual sequence of phagocytosis occurs.

(3) In an animal in which the ferments are unable completely to break down the bacterial protoplasm quickly enough, the toxic proteolytic degradation bodies are liberated and these act aggressively, inhibiting phagocytosis. If these toxic bodies accumulate at a sufficient rate the animal dies and the endothelial cells do not appear in the exudate. If, however, the toxic bodies do not accumulate so rapidly the polymorphonuclear neutrophile cells, after a considerable increase in numbers, are able, in time, to phagocytose the bacteria, and eventually the usual sequence, though delayed, occurs.

So we would say that an animal is immune to a bacterium—

(1) If the bacterium is unacted on by the ferments and so remains innocuous.

(2) If it is so rapidly broken up by the ferments present that its proteolytic degradation bodies are quickly reduced to non-toxic ones, and so it again becomes innocuous.

And an animal is susceptible to a bacterium if the ferments can split off from the bacterium toxic substances in such amount as to inhibit phagocytosis. Thus to a given bacterium an animal may have very little ferment action, so little toxic substance will be split off to act aggressively, so that phagocytosis will occur and the animal will be unaffected. If, however, the ferment activity is greater because there is more ferment, or because there is a specific ferment, or because the bacterium is more fragile, then toxic substances will be liberated in sufficient amount to act aggressively, so that phagocytosis will not occur, the bacteria will multiply, and septicæmia will ensue (or the ferment may destroy the bacterium, but may be present in insufficient amount to degrade the protoplasm sufficiently rapidly to render it non-toxic so that these toxic substances liberated will kill the animal). Further, if the ferment activity is still greater the bacteria will be rapidly degraded beyond the toxic stages, aggressive substances will not accumulate, phagocytosis will occur, and the animal will recover.

First, then, we will take organisms to which the ferment activity normally is very low, such, for example, as the *Bacillus mycoides*, a soil organism superficially resembling the anthrax bacillus, but naturally incapable of growth at the body temperature and possessing flagella; the Timothy grass bacillus; the *Smegma bacillus*.

These organisms when injected into the animal body produce in the case of the *Bacillus mycoides* no lesions (even when this organism is

educated to grow at body temperature). In the case of the Timothy grass bacillus a plastic peritonitis occurs with pseudo-tubercles, with massive doses in the guinea-pig, from which the animal recovers. The infection only proves fatal on the addition of butter, and only Rabinowitch has been able to pass the strain on subsequent inoculation, other observers repeating her work have failed. The organism produces no disease in rabbits.

A series of guinea-pigs were inoculated with 20 mg. dry weight of these organisms. In the case of mycoides, after a week it was found that the intraperitoneal inoculation of an agar slope of mycoides grown at 37° C. produced death of a sensitized guinea-pig in sixty hours. The post-mortem appearances were œdema of the abdominal wall, slightly turbid peritoneal effusion, enlargement and congestion of the spleen, liver and kidneys, moderate distension of the lungs, engorgement of the right side and veins. The organism was recovered in pure culture from the œdema and peritoneal fluid, from the spleen, gall-bladder, urinary bladder, and heart's blood. Microscopically the organism was seen in the capillaries of the spleen and liver, and was non-sporing. The post-mortem was thus indistinguishable from one of anthrax.

With the Timothy grass and the smegma bacilli an inoculation was made of one twenty-four-hour glycerine agar slope intraperitoneally into each guinea-pig correspondingly sensitized one week previously. Death occurred in from ten days to a fortnight: the post-mortem appearances were emaciation and hair falling out, miliary tubercles throughout the body, some degree of plastic peritonitis in addition to the usual pseudo-tubercles that occur with the inoculation of these organisms into normal animals. The omentum was rolled up, infiltrated, and studded with tubercles. The organisms were recovered from the heart's blood in addition to other sources. The microscopical appearances were those of marked epithelioid reaction with the organisms in the lesions, and in the centre of some of the lesions typical granular necrosis. The post-mortem appearances were thus indistinguishable from those due to an intraperitoneal injection of tubercle bacilli.

Parallel to these is an experiment in which we were able to produce acute miliary tuberculosis in a rabbit with a very small quantity of human tubercle bacilli. The rabbit was inoculated with about 0.05 mg. of human tubercle bacilli fourteen days after sensitization with 50 mg. of killed pulverized tubercle bacilli. The rabbit died in one week. In a similar way, Duval and Couret have shown that experimental leprosy lesions can only be produced in monkeys after previous inoculation with dead leprosy bacilli.

We found that the sensitive period for infection was from six to ten days after the sensitizing dose. If, however, the second inoculation is given to a sensitized animal after an interval of a fortnight instead of a week, the animal recovers and does not develop the disease, unless a much larger second dose is given than in the above experiments. Later still the animal becomes so immune that the second dose, to produce any symptoms, has now to be so large that it is only capable of producing delayed toxic death, the animal not living long enough to develop septicæmia. The reason for this is that the ferment is increasing in quantity and is becoming more specialized as the length of time from the sensitizing dose increases; and only by using the methods we are just coming to can septicæmic death be produced.

Secondly, we will consider organisms to which ferment activity is relatively high, so that the guinea-pigs are immune for this reason. Organisms of this description are Hoffmann's bacillus, *Sarcinæ*: *Proteus zenkeri*, *Staphylococcus pyogenes aureus*, *Streptococcus erysipclatis* and *Cyanogenus*.

We found that in trying to produce lesions with these organisms by the previous method we were unsuccessful, and in most of them the large initial doses of the bacilli, 10 to 20 mg. dry weight, produced death from toxæmia, with occasional terminal coli, &c., infections. From this we concluded that the available ferment present was capable of rendering non-toxic relatively large quantities of bacteria. Such being the case, we thought that if by some means we could (1) prevent the ferment getting rapidly at the bacterium, and (2) delay ferment action, we should be able to produce septicæmia with these organisms; for we should prevent the rapid breaking down of the bacteria and so allow aggressive substances to be formed. The bacteria would then be able to multiply in situ until the available ferment was so reduced that the organisms would be able to pass into and multiply in the blood-stream. To obtain this result we injected the bacteria in 15 and 30 per cent. gelatine and 2, 3 and 5 per cent. saline. The gelatine was used with the idea of delaying the access of the ferment to the bacteria, and of keeping the degradation products formed in their immediate vicinity and so produce around them a state of ferment equilibrium. The bacteria, then, as a result of this could multiply. The viscosity of the gelatine would further tend to delay the advent of the phagocytes. The gelatine might be thought to be able to produce toxic results by itself, which we found not to occur, or in adjuvanting the toxic substances formed from the bacteria, by degradation bodies from the gelatine itself. That this latter apparently is not the case can be seen from our experiments in which egg-sensitized

guinea-pigs receiving a second dose of egg albumen, so as to produce a great fall of temperature lasting for hours, were not susceptible to several slopes of staphylococcus inoculated simultaneously, though degradation bodies from the egg must have been present. The hypertonic saline, as has been shown by Friedberger and his co-workers, inhibits ferment action, and we conceived that by injecting hypertonic saline into the peritoneal cavity the ferment action would be delayed until the necessary dilution of the saline had occurred by osmosis. We will discuss the effect of hypertonic saline on the *bacteria* later. Working by these methods we were able to produce fatal septicæmia with all these organisms, but the amount of bacterial substance required was very different with the different bacteria.

The less primarily toxic the bacterium was the more was required to produce septicæmic death. Except in so far as the gelatine method can be used for demonstrating that where large amounts of ferment are presumably present the amounts of bacterial substance required to produce septicæmic death are correspondingly large, in the light of further work we do not consider the gelatine method a good one for proving immunity due to large quantities of ferment; for we have been able to produce by this method, but not by the saline, acute septicæmic death with an unpassed mycoides (growing at 37° C.). This can readily be explained. Friedberger was able to produce anaphylatoxin in the peritoneal cavity of guinea-pigs with any bacterium. We have noted that where large amounts of coagulated egg albumen are introduced into the peritoneal cavity toxic substances are formed from it, producing a fall of temperature. In the same way, similar substances can be liberated from the *Bacillus mycoides* and in the viscid gelatine, zones of ferment equilibrium become established round the bacteria, the ferment is incapable of destroying them, and by the time the delayed phagocytes arrive at the bacterium the aggressive substances prevent phagocytosis and the organism is able to survive. Thus we proved that the pathogenicity of bacteria depends upon the activity of the ferments in the animal host. If there is no, or slight, activity the organism is non-pathogenic; if there is high degree of activity, again the bacteria are non-pathogenic. And by either increasing or diminishing the ferment activity as the case may be, the bacteria may be rendered pathogenic.

Now with regard to virulence of bacteria. This must be regarded as entirely an educative property acquired by the bacterium. Gal showed that bacteria could be rendered virulent by cultivation in the presence of an enzyme, such as the enzyme of yeast cells. He further



showed that virulent bacteria could more readily undergo disintegration than non-virulent, and demonstrated a so-called antitryptic effect. We have shown that—

(1) Bacteria which are primarily non-pathogenic can, after passage through a sensitized animal, become so altered that they now produce disease in a normal animal; that is to say, they can be acted upon by the normal ferments so readily that sufficient aggressive substances are formed.

(2) That organisms which have been obtained from the blood of septicæmic animals, which are normally immune owing to the high activity of the ferment, inoculated into normal animals will produce disease and death.

(3) That some organisms when they become virulent can develop a capsule.

With regard to the first of these points, we have been able to produce disease followed by death in normal animals after inoculating with passed *Bacillus mycoides*, *Bacillus Timothy grass*, *Bacillus smegmæ*, not only in guinea-pigs in which the original passage was conducted, but also in rabbits and rats.

In the case of the *Bacillus mycoides*, it eventually became so virulent after several passages that one-twentieth of a twenty-four hours' agar slope killed a normal guinea-pig weighing 300 grm. in about thirty-six hours. One-twentieth of an agar slope killed a rat in twenty-four hours, and half an agar slope killed a rabbit in twenty-four hours. Finally, eighteen guinea-pigs which had been placed in cages in which other guinea-pigs had died from the disease all died as the result of intestinal infection. It is interesting to note that one guinea-pig which was pregnant was found to have the *Bacillus mycoides* in pure culture in the amniotic fluid.

With regard to the Timothy grass and smegma infections, the bacteria when isolated or when injected in the ground-up spleen, produced in normal guinea-pigs death with miliary tuberculosis and enlargement of the lymphatic glands in the chest in from four to twenty days. The organism has, as the result of repeated passage, now become so virulent that septicæmic death will occur in four days. The organisms when inoculated intraperitoneally into a rabbit in small quantity produce death in a week with general miliary tuberculosis, slight fibrinous peritonitis and enlarged glands, showing miliary tubercles, in the chest. This is particularly important, because lesions are not produced in the rabbit by the unpassed bacteria. With regard to the second group of



organisms, these, when passed, produce septicæmia with very small quantities without the aid of gelatine or hypertonic saline.

It was found that the *Bacillus mycoides*, which ordinarily has flagella and no capsule in the animal body, develops a capsule and loses its flagella when it becomes virulent. We will first discuss the composition and the function of the capsule. We conceive that the capsule is composed of extruded bacterial cytoplasm, which is extruded for the purpose of engaging the ferments and preventing them from reaching the bacterium itself and causing its death and destruction. It appears to us that the mechanism is to produce a state of ferment equilibrium around the bacterium, so that the bacterium is shielded from the further action of the ferment and is able to grow and multiply. Whether this is successful or not depends upon the relative amount of bacterial protoplasm and ferment activity. We are aided in this conception by the action of hypertonic saline, noted in our experiments. The hypertonic saline in addition to hindering the action of the ferment also appears to have an influence on the bacterium. The bacterium being in a hypertonic solution is subject to osmosis, the result of which is that diffusion of the bacterial cytoplasm occurs, thus forming a capsule in which the same condition of ferment equilibrium can be maintained in the presence of the weakly acting ferments. In the case of the gelatine, similar zones of equilibrium are maintained around the bacteria in the gelatine. The gelatine prevents rapid removal of the degradation bodies produced around the bacteria. It is conceivable also that the bacteria exude a little protoplasm into the surrounding medium which may be more soluble than the capsules ordinarily demonstrable. This is kept in position by the gelatine so that the necessary equilibrium zone can be maintained. This is seen in the case of our experiments with the *Proteus zenkeri*, where an unpassed strain was injected in gelatine and 5 per cent. saline. Seven agar slopes injected in 5 per cent. saline produced no result beyond a transitory fall of temperature, but four agar slopes in gelatine produced toxic death and eight slopes produced septicæmia. The difference in the two cases would appear to be due to the gelatine temporarily acting as a containing capsule preventing the removal of the aggressive substances. We would conceive that exotoxin is really this capsule formation in an exaggerated degree, but differs, in that the bacterium diffuses its protoplasm into the surrounding medium instead of retaining it in its immediate vicinity. And we regard exotoxin as soluble bacterial protoplasm which only becomes toxic on contact with ferment. The reason why we are led to conclude this is that with *Bacillus diphtheriæ*

and *Bacillus hoffmanni* a septicæmia has never been produced. This appears to us to be due to the fact that zones of ferment equilibrium do not occur intimately around the bacterium, and so the ferment, which is apparently of high activity, is able to penetrate and kill the bacteria, the animal dying of toxæmia. The proof of the high ferment activity is that the guinea-pig can withstand large doses of these organisms if inoculated in the ordinary way and that the animal does not take the disease after sensitization. Now we have been able to obtain a Hoffmann and diphtheria septicæmic death by means of the gelatine and saline methods. From this we conclude that by the gelatine method we were able to keep the exuded bacterial protoplasm in intimate contact with the bacterium, so that a zone of ferment equilibrium could be established round the bacterium, forming a protective sheath against the further action of the ferment. In the case of the saline the inhibition of the ferment action and the exudation of a greater amount, and the lessened tendency to diffusion of the bacterial protoplasm, will bring about the same result. That these animals die of proteolytic degradation body poisoning can be demonstrated by the fact that the inoculation of their blood intravenously into a normal guinea-pig produces acute toxic death (acute anaphylaxis). This brings the diphtheria bacillus into line with the other bacteria; and it shows that death from bacteria possessing exotoxin or not is always due to the same cause—i.e., proteolytic degradation body poisoning.

In order to further this view several points require explanation. How does toxin become toxoid? Toxins may be converted into toxoids by heat, by standing, by sunlight, and by drugs, such as iodine.

With regard to heat: If exotoxin is bacterial substance it will contain the autolytic ferment of the bacterium. Now on moderate warmth or standing this ferment starts degrading the bacterial protoplasm and after a time no further degradation can occur (unless the end-bodies are removed), owing to ferment equilibrium, so that at any time there will be present:—

(1) Unaltered bacterial protoplasm, which on inoculation can be converted into toxic early degradation bodies.

(2) Early degradation bodies, which on further action are rendered non-toxic.

(3) Non-toxic end-bodies.

The much smaller amount of unaltered protoplasm is more rapidly attacked by the ferment present in the animal, so that the toxic bodies only tend to be present at any time in small amount, producing local changes at the seat of inoculation and no general poisoning. On this

assumption we can also explain how it is that a toxoid can act as an antigen. Again, this explains why the fixation of complement occurs when toxin and antitoxin are added together (Nicolle and Armand Delille), for we must consider the antitoxin as a co-enzyme or ambceptor. Then with regard to the difference between the L0 and the L+ dose: on the principle on which these are worked out, no account is taken of the normal active ferment present in the guinea-pig.

Chemicals, such as iodine, converting the toxin into toxoid: We have the observations of Friedberger and Schittenhelm that iodized albumen can act as an absolutely foreign proteid to the homologous animal, so that iodine acting on bacterial protoplasm may so alter it that the ferments which could easily attack the ordinary toxin can now only very slowly act on the iodized "toxin." But as we know iodized toxoid can produce antitoxin, that is, a ferment against the unaltered toxin; this is parallel to the observation of Schittenhelm, that guinea-pigs sensitized against iodized egg albumen can react not only to that but to plain egg albumen. This means that the newly evolved ferment can also degrade the non-iodized homologous proteid.

Though we have discussed so far pathogenicity and virulence separately, yet we have come to the conclusion that they must be considered together. Thus an organism by passage may become so altered that it is able to infect and multiply in an animal in which there is no specific ferment. The mycoides could only become pathogenic in the first instance on inoculation into a sensitized animal, that is, an animal that has acquired a certain amount of specific ferment. After passage this organism is capable of producing disease in a normal animal, that is, an animal which only contains panenzyme. Hence we must conclude that the bacterium has become so altered that it can be attacked by the panenzyme at such a rate that sufficient aggressive substances are formed to prevent phagocytosis, and that it has developed the property of extruding a capsule to form a protective zone in which ferment equilibrium occurs to prevent the enzyme from penetrating and destroying it. Thus we see that a bacterium which is virulent may also be pathogenic. The passed *Smegma* and *Phlei* are similar.

Now we must consider the bacteria which are not under ordinary circumstances pathogenic and which do not become so when the ferment is raised against them by the production of specific antibodies. The first point we must discuss is the *activity of the ferment*. We have come to the conclusion that septicæmia is not produced by a process of general ferment equilibrium in the whole animal body, but that septicæmia occurs if the relation between the quantity of bacterial proto-

plasm and the ferment activity is such that aggressive substances are formed from the bacterial protoplasm by the ferment in sufficient amount, and remain as such long enough to inhibit phagocytosis.

Now first of all we can compare *in vivo* experiments with experiments carried out in the test-tube. From theoretical considerations the quantity of ferment only influences the rate of degradation, not the amount. So that *in vitro*, no matter how much ferment is present, ferment equilibrium eventually takes place and the same amount of the undegraded material remains in the two cases. This would mean unaltered bacterial protoplasm. We know from experiments *in vitro* that under these conditions, after ferment equilibrium has occurred the bacteria start to multiply again. Now, taking two guinea-pigs with the same quantity of ferment, if in one the ferment activity is unaffected, and in the other the ferment activity is damped, and into each the same amount of living bacterial protoplasm is inoculated, ferment equilibrium should occur in both, and septicæmia, if it occurs in one, should occur in the other, but at different times. But we find that where the ferment has been damped septicæmia occurs and not in the other; hence we must conclude that septicæmia is not produced by general ferment equilibrium in the animal body alone. Taking account also of rate of removal of end-bodies in both cases, these are being gradually removed, in the one case more rapidly than the other; so that in both cases, theoretically, if the amount of ferment is sufficient, the primary substance should be completely broken down. Hence we must conclude that the occurrence of a septicæmia depends upon the presence at any given time, and the maintenance, of early degradation products sufficient to prevent phagocytosis. Where the ferment activity is great the accumulation of the aggressive early degradation bodies is temporary, so that the inhibition of phagocytosis is only temporary, and this ceases directly the bodies are further degraded.

Finally, there remains for discussion the fact that these organisms, which by our methods have produced septicæmia, are now able when directly inoculated into a normal animal, and in much smaller doses, to produce septicæmia. The fact that they can do so is a great argument against fermentative equilibrium being the sole cause of septicæmia. Taking two normal animals and inoculating the same quantity of passed and unpassed bacteria, in the former septicæmia occurs, in the latter nothing. Here the factors are the same: the same activity, the same weight of bacterial protoplasm; hence if septicæmia were solely due to general ferment equilibrium septicæmia should occur in both. Hence we conclude that the difference is due to the retention around the

passed bacterium of bacterial protoplasm in various stages of degradation forming on the one hand an aggressive shield against the phagocyte and on the other hand against the ferment, so that the bacterium can multiply. Here, again, we believe that a bacterium which is virulent is so in virtue of its being able to exude some of its cytoplasm around itself and not into the surrounding medium, and we should expect that on these lines a diphtheria bacillus which became virulent would not produce soluble exotoxin, but keep its halo of bacterial substance around itself. That this is probably so is brought out by the well-known observation that a very virulent diphtheria bacillus produces very little exotoxin.

#### CONCLUSIONS.

(1) Ferments form an important normal mechanism of defence against bacterial invasion. The ferments performing this important function are: (a) The normal panenzyme; (b) the slightly differentiated specific enzyme; (c) the thermolabile specific co-enzyme or amboceptor; (d) the thermostable specific co-enzyme or amboceptor. These last two adjuvant and accelerate the action of the ordinary enzyme. The action of the ferment is to bring about proteolytic digestion of the bacteria.

(2) Exotoxins and endotoxins are bacterial protoplasm and are not primarily toxic *per se*, but only become so when acted upon by the ferments.

(3) The action of the ferments on the bacterial protoplasm is to produce toxic early proteolytic digestive bodies. These bodies, besides being toxic to the animal, are also aggressive in the sense of Bail—i.e., are anti-phagocytic.

(4) The action of this toxic substance besides being aggressive is to produce: (a) in large amounts, death; (b) in lesser amounts, fall of temperature; (c) in small amounts, fever. This substance is the cause of death in all bacterial infections.

(5) The virulence of a bacterium is dependent upon the power of exuding around itself a zone of its cytoplasm, which remains in position and acts as a protective shield. The production of a zone of ferment equilibrium in this shield protects the bacterium itself from the penetration of the ferment. The shield thus acted upon is also aggressive to phagocytosis.

(6) Pathogenicity is due to: (a) the virulence of the bacterium; (b) the relative activity of the ferment to the bacterium.

Thus we should say that immunity is due to phagocytosis and ferment action, that is to say, cellulo-humoral.

## Pathological Section.

February 18, 1913.

Dr. R. T. HEWLETT, President of the Section, in the Chair.

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### A New Method for the Differentiation of certain of the Streptococci.

By H. WARREN CROWE.

IN my communication of last March<sup>1</sup> I described the remarkable growth exhibited by certain streptococci isolated from urine on a modified form of Dorset's egg medium. These organisms produced in their growth colonies of a characteristic colour and shape; one was flat and remained yellow, another resembled a flattened cottage loaf and became crimson. They could be recognized when isolated by their macroscopic appearance. The scope of this inquiry has been extended; the colonies of many streptococci have been scrutinized, and in the result the medium has been found to provide a valuable help in differentiating members of this group.

The recipe for the medium differs only from Dorset's in that the process is carried through in sterile fashion, and, as suggested by Fleming, neutral red is added as an indicator; 0.005 per cent. is the proportion which I use.

The exact method of procedure is as follows: A large flask, stoppered by a cotton-wool plug, into which the requisite amount of neutral red has been introduced, is autoclaved, together with two rubber corks, each bored with two holes. One cork, which I will call A, is fitted with a couple of glass rods or wires with cross-pieces, the ends of which,

<sup>1</sup> *Proceedings*, 1912, v, p. 159.



when pressed home, will extend to within 1 in. of the bottom of the flask. Through the other cork, B, there are passed two glass tubes, the one inserted so far as to reach nearly to the bottom of the flask, the other 2 in. or 3 in. only from the cork. That part of the former which will be outside the flask is bent so as to form a recurved angle, lightly plugged with cotton-wool, and fitted with a short rubber connexion, whilst the shorter piece of tubing is joined up with a hooded pipette for conducting the medium into tubes or plates, as may be required. A clip is attached to each. Fresh eggs are then soaked in spirit; the flask is removed from the autoclave and the eggs are taken in turn, flamed, cracked at each end by a long pair of sterile sinus forceps, and placed in succession on the top of the flask, the wool plug having been removed. Each egg will be found to discharge quite readily into the flask if the forceps are pushed through the cracked ends, partly withdrawn, and then opened wide in the interior of the egg to break the yoke. When the contents of the eggs have been successfully manœuvred into the flask, cork A is removed from the autoclave, and in its turn replaces the shell of the last egg. After a thorough shaking has produced a satisfactory emulsion, cork B is removed from the autoclave, substituted for cork A, and securely tied in position. The clips are adjusted, the flask turned upside down and suspended. The long tubing reaching to the bottom, now the upper end of the flask, acts as an air valve, and to hasten the flow of the otherwise somewhat sluggish emulsion, a Higginson syringe bulb can be attached to this tube to increase the air-pressure when required. After an interval to allow all pieces of shell or unemulsified albumin to sink below the top of the shorter tube, the medium is run into sterile tubes or plates, which are laid respectively in serum racks or flat trays. Finally, the finished product is gained by heating to 90° C. for half an hour, or by steaming for the same time. If plates are desired, it is important to enclose some absorbent under the lid of the plate, such as sterilized blotting-paper, to prevent water of condensation from dripping on to the medium. Finally, the medium should be dried off in the hot oven at 60° to 70° C.

When examining streptococci grown on neutral red egg medium regard must be paid to (1) the colour of the colony (Plate, fig. 1); (2) the shape of the colony (Plate, fig. 2); and (3) the effect, if any, on the surrounding medium. Of these, the shape of the colony is the most important, and to see this properly a hand lens should be employed with reflected light, but it must be understood that unless the consistency of the medium is correct characteristic colonies may not



appear. If the medium is too moist, distortion may take place by reason of the colonies spreading, whilst, on the other hand, if the medium is too dry the growth will be wrinkled and stunted. A platinum wire should not be able to cut the medium, but the surface should be elastic and recover from the pressure of the needle. Special care must be taken, before forming an opinion, that sufficient time has elapsed for full development, and this may be favoured by keeping the culture at room temperature, or in a cool incubator for several days after incubation at 37° C. Experience, however, will frequently enable one to determine the type of streptococcus within forty-eight hours or less. The best results are obtained by examining recently isolated germs; old cultures are apt to lose their characteristic colonies.

The value of the medium as a means of differentiation is diminished by the fact that some streptococci grow but feebly or not at all. Yet importance attaches to this negative property, for the non-growers are chiefly confined to streptococci isolated from sputum. The division of the streptococci into two groups, A and B, according to the presence or absence of growth on egg medium, corresponds then to a natural classification in respect of their habitat, though there are four notable exceptions to group A:—

(1) The pneumococcus, usually grows fairly profusely; rarely may not grow at all.

(2) The *Streptococcus mucosus*.

(3) A small lanceolate streptococcus, which frequently appears capsulated.

(4) Streptococci such as are found in the mouth.

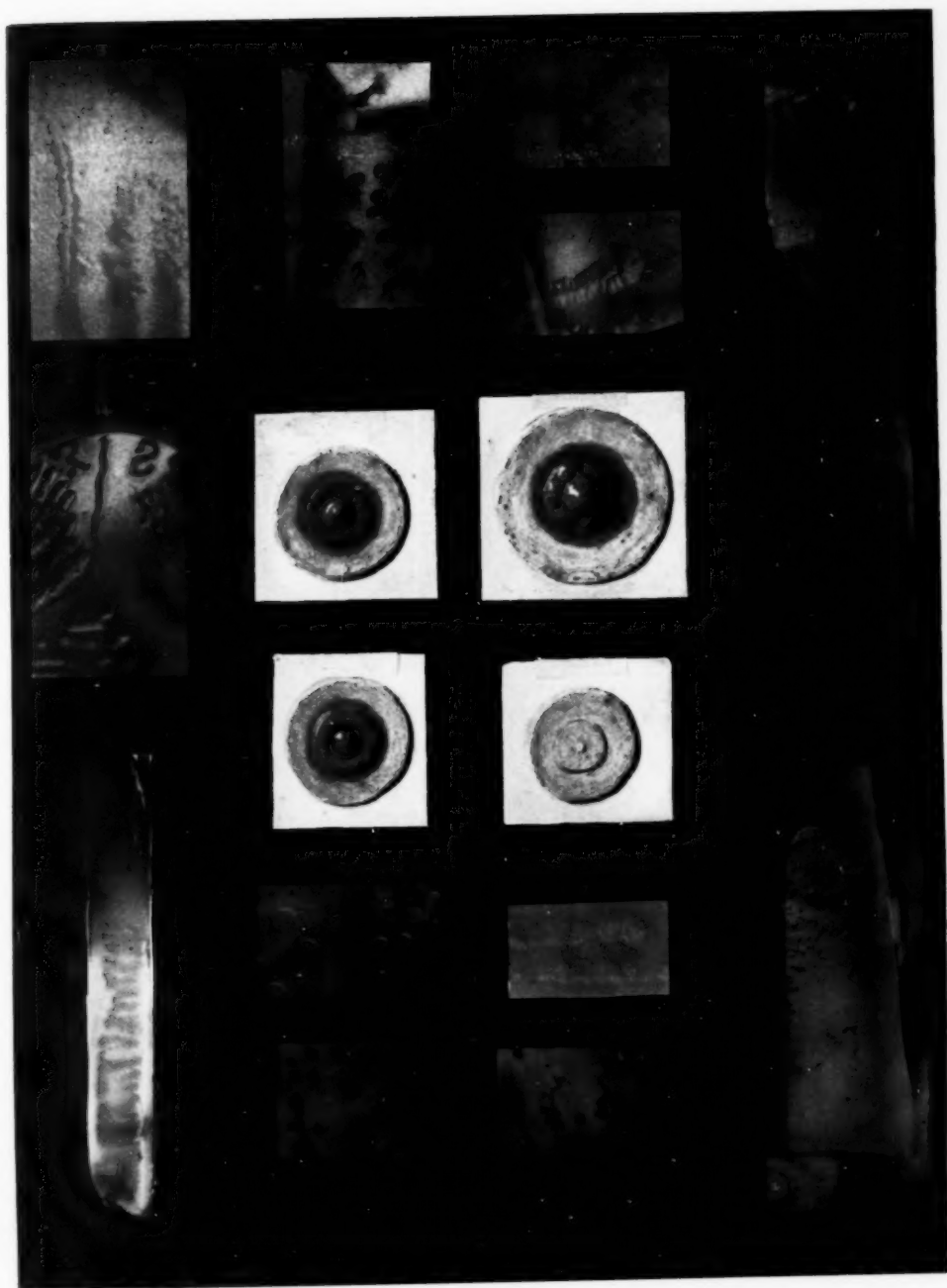
All these give perfectly distinctive colonies on egg medium.

(1) The colony of the pneumococcus is yellow. In its earliest growth a small bump appears; a minute dimple then begins to show itself in the centre of the bump, and finally there develops a small ring with a raised edge and a raised centre.

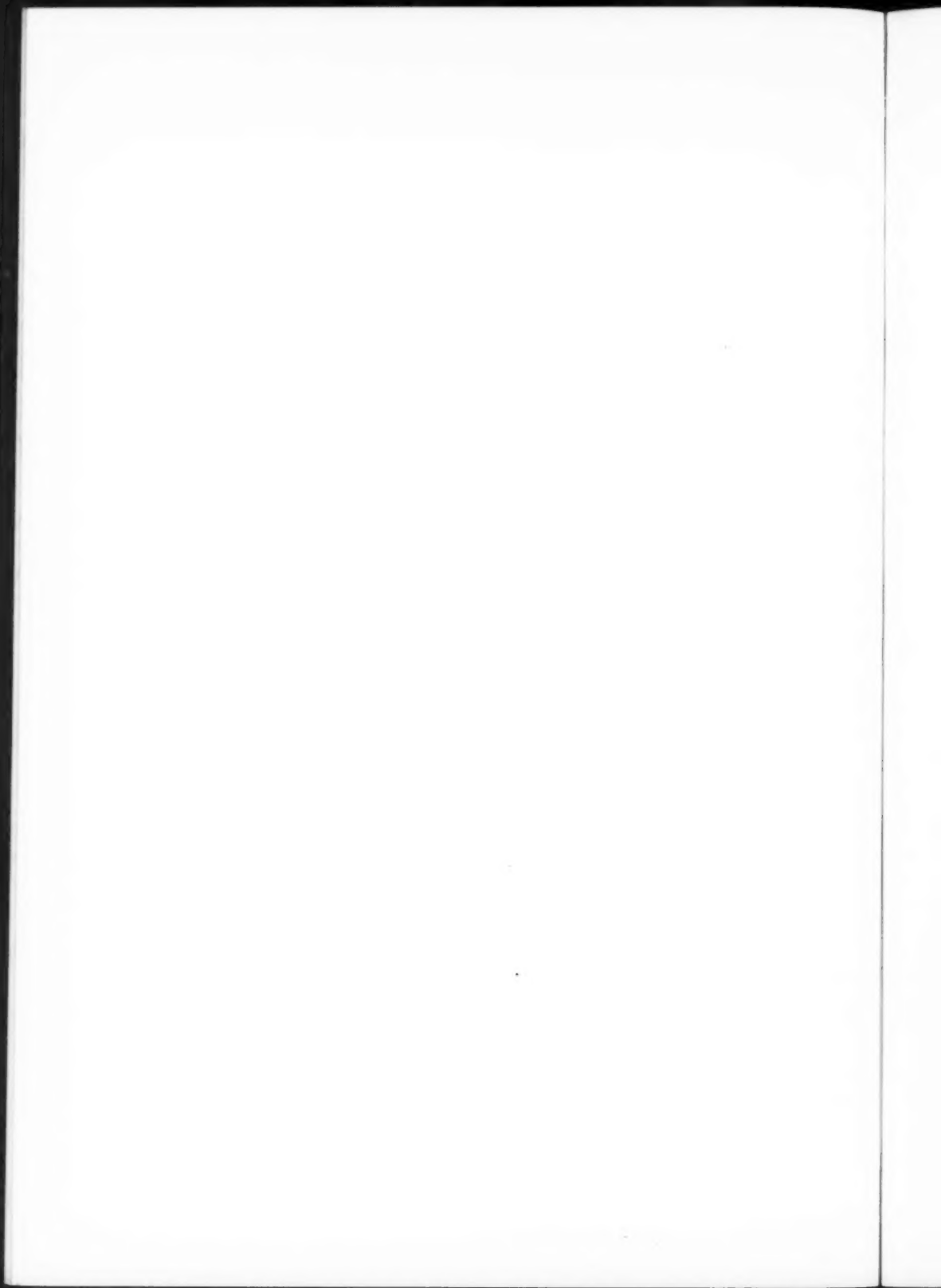
(2) The *Streptococcus mucosus* has frequently been thought to be a variation of the pneumococcus; nevertheless the colonies on egg medium are totally different. They are large, slimy-looking masses like drops of rain-water, which may grow to a size of over a quarter of an inch in diameter during twenty-four hours. Colour reaction varies. Some strains remain yellow, others become rose-pink without affecting the medium, others, again, turn the medium a light crimson, and assume the same colour themselves, but the shape and general appearance of the colony is the same. This organism, commonly called the

EXPLANATION OF THE PLATE.

- FIG. 1.—Twenty-four hours' culture of *Streptococcus faecalis* on neutral red egg medium. Where the organism is growing crimson streaks are produced.
- FIG. 2 is placed in the centre of four plaster casts of models of streptococcus colonies. The upper right-hand model shows "cottage loaf" type; the upper left-hand model the "broad-brimmed hat" type; the lower left-hand model the "draughtsman" type; the lower right-hand model the flat colony.
- FIG. 3.—*Streptococcus mucosus* (forty-eight hours); faint indication can be seen of large, slimy colonies.
- FIG. 4.—Twenty-four hours' culture of *Streptococcus mucosus* II; note plum-coloured blush.
- FIG. 5.—*Streptococcus mucosus* II; original culture on an egg plate direct from sputum. Note brilliant plum-coloured spot in centre of "cottage loaf" colony.
- FIG. 6.—*Streptococcus mucosus* II, after several subcultures, colonies ringed; the colour is now a pale puce.
- FIGS. 7 and 8.—Young and old cultures of the *Streptococcus salivarius* of the type "flat colony" seen immediately above them. The former was isolated from acute tonsillitis; the latter is Professor Beattie's strain No. 48.
- FIG. 9.—*Streptococcus faecalis*; smooth "cottage loaf" type, isolated from the urine in chronic rheumatism.
- FIG. 10.—*Streptococcus salivarius*; ribbed and fluted "cottage loaf" type, from a culture sent to me by Dr. Gordon. Immediately below fig. 10 is the type model "cottage loaf."
- FIG. 11.—*Streptococcus salivarius*; the "broad-brimmed hat" variety (most frequent in pyorrhœa). The type model is immediately beneath it. Professor Beattie's strain No. 7.
- FIG. 12.—*Streptococcus pyogenes*; the "draughtsman." Note similarity to model next above it. A culture from Dr. Gordon.
- FIG. 13.—*Streptococcus pyogenes*; a variety producing a smaller colony, but otherwise the same. A culture from Dr. Pethybridge.
- FIG. 14.—Three "indenting" streptococci as described in text. The high lights show that the medium is markedly pitted where growth occurs.



WARREN CROWE : *New method for differentiation of streptococci.*



*Streptococcus mucosus* in this country, is probably identical with that known as the *Streptococcus epidemicus* in America. A culture of the latter, sent to me by Dr. Winslow, of the American Museum of Natural History, produced these characteristic colonies (Plate, fig. 3).

There is, however, another smaller organism, which I call tentatively *Streptococcus mucosus* II, and to which a capsule cannot always be demonstrated. Of all streptococci, the *Streptococcus mucosus* II possesses the most distinctive colony. It is shaped somewhat like a flattened cottage loaf, and is of a pearly-grey appearance. It does not as a rule colour the surrounding medium to any great extent, but the central portion, that is to say the upper or smaller part of the loaf, appears when viewed by direct light to be of a brilliant plum colour. If sputum in which this organism occurs—and it is extremely common—be smeared on an egg plate, the colony can be picked out after twenty-four or forty-eight hours' growth by the naked eye from amongst a host of others, on account of this characteristic appearance of a plum-coloured spot (Plate, fig. 5). Figs. 4 and 6 in the plate show young and old subcultures.

The mouth streptococci more properly should be included in Group B, as they are not, I think, lung streptococci proper. In Group B there are two main divisions: (I) Yellow colonies; (II) crimson colonies. The latter appear to be the most important. I cannot say much about the former. The only examples I can quote are:—

(1) The *Streptococcus equinus*. The few examples of this organism which I have examined all show a typical cottage loaf colony.

(2) Certain small diplococci in the mouth.

(3) A streptococcus which usually produces but little if any crimson coloration, until after continued growth. It is most frequently isolated from the tonsils, though I have found it occasionally in urine. It was described in my paper last March as the *Streptococcus (?) salivarius*. From observations on patients under vaccine treatment this organism possesses a considerable degree of pathogenicity. The colony is large, very flat, circular or irregular in outline, and stippled, or covered by fine rings. Professor Beattie kindly sent me six cultures of the strains of streptococci with which he had produced arthritis in rabbits, and one of them, isolated from the tonsils, was of this variety. Morphologically the chains are fairly long (Plate, figs. 7 and 8).

(II) Colonies crimson, medium crimson: the majority are streptococci from the human alimentary canal. In the group of alimentary streptococci we find three fairly clearly defined types of colonies, all

more or less producing crimson, and in addition the flat colony described (1, 3). As might be expected in streptococci inhabiting the alimentary canal, there is a close family resemblance between them. The youngest colonies are simply small bumps, which in their growth develop a papilla.

Varieties are distinguished by their subsequent behaviour:—

(1) The papilla flattens out, but keeps pace with the growth of the rest of the colony, which remains smooth and regular. The appearance is that of a smooth cottage loaf. This is the *Streptococcus faecalis*; it is the organism most frequently found in the urine of chronic rheumatism, and was described in my paper as the diploid streptococcus. Professor Beattie's strain, No. 125, which was isolated from an appendix, produced this colony. Morphologically chains are very short; individual cocci are egg-shaped, and lie, as a rule, with their long axes parallel (Plate, fig. 9).

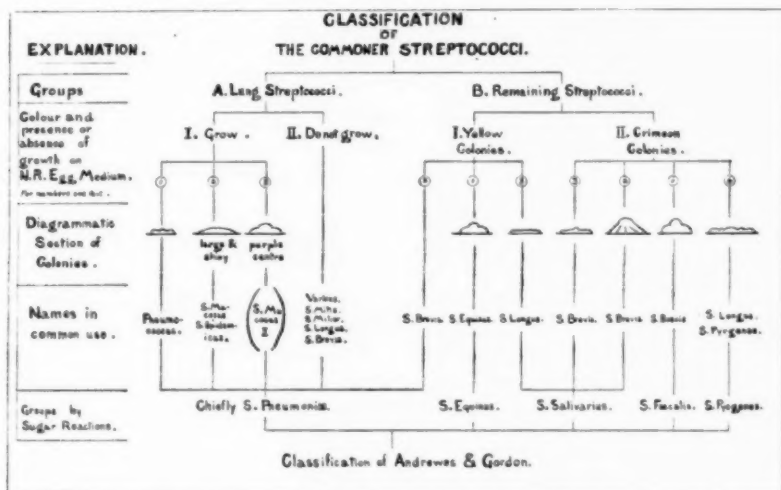
(2) This variety is also of the cottage loaf type, and unless the medium is very good cannot be distinguished from (1); yet there is a definite difference to be noted in that the larger part of the loaf (the base) becomes ribbed or fluted. It is found in the sputum in chronic bronchitis, but probably as an accidental infection from the mouth where its occurrence is frequent. Its pathogenicity as a sputum organism is doubtful. None of Professor Beattie's strains grew in this manner, nor have I found it in rheumatic urines. The *Streptococcus salivarius* sent to me by Dr. Gordon gave this colony; it was isolated from an appendix abscess, but whether present in pure culture I do not know (Plate, fig. 10).

(3) The papilla remains small and round, whilst the rest of the colony grows and spreads out; thus is produced the "broad-brimmed hat." This variety is frequently isolated from cases of pyorrhœa. Several of Professor Beattie's arthritic strains produced this colony. It is remarkably constant, easily recognized, and is given by old subcultures. It is frequently found in the urine of patients suffering from indefinite rheumatic symptoms (Plate, fig. 11).

(4) The *Streptococcus pyogenes* in my experience provides one of the prettiest and most easily recognized colonies. Take a "draughtsman," paint it crimson, embed it in a flat plasticine surface, and you have the type of colony assumed by this organism. Under certain conditions the resemblance is remarkably striking, on account of the neatness and definition of the ridges and depressions. I regret that the illustrations do not show this characteristic, but frequently when one particularly wants a good specimen it fails to make its appearance. After many subcultures the colony seems to lose its characteristic shape, and it

may be impossible of recognition. I cannot say if there is another form of *Streptococcus pyogenes*: this certainly is the commonest (Plate, figs. 12 and 13).

(5) A streptococcus which indents egg medium. Many staphylococci indent egg medium, streptococci quite exceptionally. Dr. Winslow sent me a streptococcus which he named the *Streptococcus gracilis*, and described as a gelatine-liquefying streptococcus. I was under the impression that such were saprophytes. The characteristic of this organism on egg medium was indentation. One of Professor Beattie's rheumatic strains, isolated from a case of malignant endocarditis, behaved



in exactly the same way, both as regards gelatine and egg medium. A few days later Dr. Solly sent me a streptococcus for diagnosis. It was isolated from a case which clinically might be malignant endocarditis. This organism indented the medium, as can be seen on the plate, though not so markedly as the former two. Gelatine, however, was unaffected (Plate, fig. 14).

(6) The *Streptococcus anginosus*. I have not been able to obtain a culture recently, but I am under the impression that this organism also has a distinctive colony.

The classification of the streptococci has always been somewhat unsatisfactory, and the more so because of the great variety of diseases to which these organisms can give rise. The morphological



classification of Lingelsheim for a long time held the field. Then there came Dr. Andrewes's and Dr. Gordon's valuable classification by the sugar reactions, which gains probability from the fact that the streptococci thus divided fall more or less into groups, coinciding with their natural habitat: faecal, salivary, connective tissue and those affecting the organs of respiration.

In reviewing my experience of the growth of streptococci on neutral red egg medium, I find that the Andrewes-Gordon classification provides a good working basis, inasmuch as streptococci thus divided present characteristic colonies, but I would suggest that by the use of this differentiating medium further definite subdivisions can be introduced. Thus the *salivarius* group should be subdivided into three—according as the colonies are flat and yellow (I, 3), or resemble a cottage loaf with fluted edges (II, 2), or a broad-brimmed hat (II, 3); the pneumococci into two or perhaps three—viz., the pneumococcus, *Streptococcus mucosus* and *Streptococcus mucosus* II; whilst the "lung" streptococci, which grow but feebly, or not at all, on egg medium, may require to be placed in a class apart. Such an arrangement of the latter might well correspond to a natural division, for streptococci, which produce disease in the lungs, broadly speaking, may be found to be air-borne, whereas other pathogenic streptococci may be water-borne. In the table I have tried, however tentatively, to bring these various classifications into line.

The chief varieties capable of causing arthritis, both in rabbits and also in the human subject, are I, 3, II, 1, and II, 3, designated the flat colony, the smooth cottage loaf, and the broad-brimmed hat. In my paper of last March I suggested that the second organism was the probable cause of chronic rheumatism, but during the discussion the opinion was expressed that I was casting an unwarrantable aspersion on a harmless saprophyte. Some degree of pathogenicity, and potentially of extreme virulence, must, however, be allowed to these short-chained organisms. The fact that one of Professor Beattie's streptococci, which produced arthritis in rabbits, gave the same colony, and was isolated from an acute case of disease, is strong evidence in support of my claim. Still stronger evidence is afforded by the converse experiment, for Professor Beattie injected rabbits with two of my strains isolated from patients suffering from chronic rheumatism, but otherwise healthy, and produced arthritis. The cultures were selected because they gave the typical cottage loaf colony on neutral red egg medium.

The organism described by Poynton and Paine, and occasionally referred to as the *Diplococcus rheumaticus*, would probably give a colony

of the cottage loaf or broad-brimmed hat type, but despite my efforts I was unable to obtain a culture.

In conclusion, I must express my most sincere thanks to Professor Beattie for sending me his rheumatic strains, and also for his kindness in injecting rabbits with my cultures; to Dr. Gordon for typical streptococci of his four main groups, "hall-marked," if I may use the term; they were most helpful to me in bringing my classification into line with his valuable work; to Dr. Ainley Walker for the contribution of his original strains; unfortunately, his manipulated cultures had been destroyed, or it would have been most interesting to have contrasted the evolved varieties; to Dr. Ledingham for sending me a series from the Lister Institute; to Dr. Solly and to Dr. Pethybridge for sending contributions of various streptococci; and very particularly to Dr. Winslow, of the American Museum of Natural History, for a splendid series of eight named varieties. Unfortunately the journey proved too long for the *Streptococcus conglomeratus*, *Streptococcus mitis* and *Streptococcus mucosus*, the death of the last-named especially being to me a matter of regret, as it is obvious that the organism named by Dr. Winslow *Streptococcus epidemicus* is identical with our *Streptococcus mucosus*. To what, then, would the *Streptococcus mucosus* of America correspond? My thanks are also due to Mr. Grant, the English proprietor of the Lumière process, and to Mr. Stoneman, photographer, of Plymouth, to whom I am indebted for valuable advice in preparing the autochrome plates, by which the shape and colour of the colonies are illustrated.

### Occlusion of the Inferior Vena Cava, as a result of Internal Trauma (Dissecting Varix ?).

[*The case of the late Dr. W. Rivers Pollock.*]

By S. G. SHATTOCK.

THE parts which form the subject of this communication were bequeathed to the Royal College of Surgeons, for dissection, by the late Dr. W. Rivers Pollock, at the time of his death (1909) Obstetric Physician to the Westminster Hospital; and this he did, by reason of the singular, if not unique, clinical history connected with his disease. I may first give the latter, then describe the specimen, and finally make a short comment on the case.

#### HISTORY.

In 1884, Pollock, when aged about 24, and in a condition of perfect health, won the 120 yards hurdle race in the Cambridge University Sports—sixteen and one-fifth seconds. In the same year he ran successfully for Cambridge against Oxford, performing the same feat in sixteen seconds. He held his breath during the whole time. This record has since been equalled, and was broken in 1907 by W. Powell, of King's College, Cambridge. Immediately after the race was over he lay on the grass, and within a few seconds complained of pain in the lumbar spinal region. He was put to bed, where he remained for six months. Œdema of the legs, and to a lesser degree of the abdomen and scrotum, supervened at once, and persisted for the period mentioned. Whilst in bed the superficial veins began, within a few days, to dilate, and their enlargement slowly progressed. During the rest of life the distended veins were supported by the systematic use of carefully adjusted elastic pants, reaching as high as the thorax. Albuminuria appeared directly after the event, and persisted throughout life. Death occurred on October 5, 1909—twenty-five years later. Mr. Arthur Evans, who attended the patient during the last six years of his life, informs me that he was subject to attacks of phlebitis and thrombosis in the enlarged saphenous veins, these attacks being readily brought on—e.g., by the pressure of a crease in the elastic pants. On September 25,

1909, the patient noticed some tenderness and discoloration behind the right internal malleolus; this extended to the dorsum of the foot. On the 29th the temperature was found to be 100° F., and he had a slight rigor. The next day his throat became sore, and on October 1 the signs of well-marked tonsillitis appeared, the lesion on the foot having vanished. The throat became more painful, and the temperature kept up. On October 4 the right tonsil was freely incised under gas; not more than three or four drops of pus escaped. Death took place on the day following, and was attributed to tonsillitis and septicæmia. Dr. J. M. Bernstein, who made the autopsy, tells me that although carried out within six hours of death, there was such a degree of generalized emphysema as to render a satisfactory examination of the viscera impossible.

#### DESCRIPTION OF THE SPECIMEN.

The preparation comprises the superior and inferior venæ cavæ, wanting their cardiac terminations. The right azygos vein, the end of which is shown entering the superior cava, is considerably dilated. Except for its highest part, the whole of the portion of the inferior cava preserved is converted into a flat, impervious ribbon, which is most contracted and thinnest for a distance of 6.5 cm. (2½ in.) opposite to and below the renal veins. Portion has been cut away from the front of the vessel below the veins last named to show that its lumen is completely occluded. The common iliac veins and the parts of the external and internal preserved are likewise flattened and obliterated, though somewhat less reduced in size owing to the presence of internal adherent coagulum. The tributaries and trunk of the left renal vein are pervious, although, as tested with the probe, the entrance of the latter into the cava is closed; the same is true of the trunk of the right renal. The right spermatic vein, as far as its entrance to the cava, is likewise pervious. From the left side of the lower part of the cava there projects the occluded end of one of the lumbar veins of the same side. The upper divided end of the inferior cava is pervious, though reduced in size. It was found during the dissection that the hepatic veins were unoccluded. The return of blood from the kidneys must have taken place through the veins of the capsule and thence by way of the lumbar through the azygos vessels.

## REMARKS.

Occlusion of the inferior vena cava as a result of infective thrombosis is a well-known condition, and not a few examples of it have been met with, the thrombus extending into the main trunk from some of its tributaries; either from the femoral and iliac veins below (e.g., in typhoid infection) or from the hepatic veins above. Occlusions arising from the direct invasion of the wall by new growth or by the extension of malignant tumours of the kidney along the renal vein are likewise well recognized, though rare occurrences in pathological anatomy. Any suggestion of such an infective origin in the case under notice, however, is excluded by the history. It is incredible that an infective disease should have been present in an athlete in such perfect condition as to have accomplished the feats recorded. Contrast it, for example, with the following, which lately came under the care of Dr. C. R. Box, at St. Thomas's Hospital: A man, aged 21, ten weeks before his admission to the hospital, fell out of health and had a rigor, which he attributed to a bicycle ride. During the next five weeks the rigors recurred on two or three occasions; finally he fainted whilst at work. Swelling of the abdomen followed, and 5 pints of serum were removed. When admitted on September 6, 1912, he was suffering from ascites and enlargement of the liver; there was no evidence of nephritis. Paracentesis on September 10 was rapidly followed by re-accumulation. The abdomen was opened, but no cirrhosis or tubercular disease of the peritoneum were found. There was no appreciable œdema of the legs. Death occurred with dyspnœa and cyanosis on September 23. He had no rigors whilst in the hospital, but there was slight fever of remittent type. The urine contained a trace of albumin. The autopsy revealed an adherent thrombus, with softened centre, in the inferior cava behind the liver; the cava below was filled with more recent non-adherent clot, which did not entirely occlude it. The clot did not reach into the iliac veins, but superiorly it extended for a short way into the right auricle. Organizing thrombi were found on microscopic examination in the hepatic veins throughout the liver. The portal vein and its tributaries were normal. The liver, spleen, and kidneys were congested; the lower lobes of both lungs were the seats of pale infarcts.

In Dr. Pollock's case the occlusion of the cava arose under such exceptional circumstances as to indicate some exceptional factor in its ætiology. And the hypothesis which I venture to put forward is, that in consequence of the extreme distension of the inferior cava occa-

sioned by the holding of the breath throughout the race, a localized rupture of the intima, or of this and the media, took place, which was followed by the forcible extravasation of blood into the walls of the vein, whilst, i.e., the exertion was still in progress; that the lesion in short, in the initial stage, was the counterpart of a dissecting aneurysm of the aorta.

Since by classical usage the word aneurysm is confined to arterial dilatation (Galen), whilst swelling of the veins has, from the time of Celsus, been known as *varix*, the term "dissecting varix" would be that best suited to meet the condition supposed. The initial lesion would be like that of a dissecting aneurysm, but the two would soon lose their resemblance. In the case of the aorta the internal pressure is maintained, and the dissection may proceed to great distances, the blood in most cases finding its way again into the arterial system through a consecutive and more distant rupture of the intima; and the intramural channel, if death does not ensue, becoming lined with organized coagulum and converted into an adventitious collateral. In the case of the vein, on the relief of the abnormal internal pressure, further extravasation into the wall would cease—the normal intracaval pressure would be too low to prolong it. But as a result of the intramural extravasation the calibre of the vein would be so reduced, if not actually closed, that secondary thrombosis would take place which would eventually occlude the channel.

All the nucleated cells of the body are capable of furnishing thrombo-kinase. And, after the partial rupture supposed, the ferment would be furnished by the injured tissues as well as by the leucocytes. From the intramural clot the coagulum would extend at the site of the rent into the diminished lumen of the vein and so bring about its complete occlusion. The intramural coagulum would subsequently undergo a transformation similar to that occupying the lumen; and, in process of time, become indistinguishable from the proper coats of the vessel.

The transverse rent of the intima and media that is so readily produced in the aorta or other artery by the application of a tight ligature, or by compressing the vessel transversely in a Spencer Wells's forceps, is not producible by the same violence in the cava or other vein. This difference is to be explained mainly by the direction of the muscle-fibre. In the case of the artery the ligature sinks without much resistance into the media by displacing its circular fibres, the externa remaining intact; the intima is ruptured last. This can be shown by tying an aorta upon a test-tube. If the force used is not extreme, it will



be found, on slitting up the artery and examining the cut edge with a hand lens, after making gentle longitudinal traction, that the externa and intima are intact, whilst the media is cleanly ruptured.

In the larger veins like the cavæ and iliacs, the longitudinal disposition of the chief part of the musculature, whether on the inner or outer side of the circular fibres, together with the admixture of white fibrous tissue with the muscle, prevents the ligature from penetrating in the same way.

The inner coats of a vein can be ruptured, however, by internal tension. If a pair of lithotomy forceps is introduced into the common iliac vein, or the cava, and slowly opened out until a rending sensation is felt, it will be found, on slitting up the vessel, that the inner and middle coats present one or more longitudinal ruptures, the external remaining intact. This is the lesion that I presume occurred in Pollock's case.

This view will commend itself the more if one endeavours to picture what the condition of the inferior cava would be in the particular circumstances under which the accident occurred. In the *first* place it is an old observation (known as Müller's) that if a prolonged inspiratory effort is made with the mouth and nostrils closed, the negative pressure, or *vis a fronte*, so induced within the thorax results in such a filling of the intrathoracic veins, systemic and pulmonary, and of the two auricles (the lungs being unable to expand and aid in filling the potential space) that the auricles become over-distended, and rendered incapable of efficient contraction; and this to so high a degree that the pulse becomes imperceptible. The embarrassment of the auricles is due not to excessive internal pressure, but rather to the fact that their musculature is too weak to enable it to cope with the negative pressure acting without, for the ventricles may continue to beat, although as they are receiving little or no blood, none reaches the systemic arterial system. *Secondly*, in the converse observation (Valsalva's), a prolonged forcible expiratory effort, with a closed airway, will likewise stop the pulse by reason of the general compression of the thoracic viscera. Professor A. Keith<sup>1</sup> has pointed out that the venæ cavæ with the innominate, iliac, hepatic and renal veins, being closed off below by the valves in the common femorals, and above by those in the subclavian and jugulars, constitute a cistern or reservoir which may be filled from its tributaries, but which can only empty itself through the right auricle.

<sup>1</sup> Structures concerned in the Production of the Jugular Pulse," *Journ. of Anat. and Physiol.*, 1908, xlii, p. 1.



In Pollock's case, so far as the *vis a tergo* is concerned, it is clear that the influx into the cavæ, or the venous cistern, would reach its highest mark, seeing that the active muscular contractions of the limbs and trunk would drive the blood through the peripheral tributaries into the reservoir without its being able to return. Some reflux through the hepatic veins by way of the capillaries of the liver, into the main, and valveless trunks of the portal system might occur, though this would be limited by the comparatively short space of time the effort lasted, and by the general compression of the abdominal viscera, maintained by the contracted condition of the parietes. But the state of things within the thorax is not so easily determinable. The chest, it is true, was in the expanded position, but dynamically the condition was one of forced expiration prevented by the closure of the airway; in addition to this there would be the less important positive pressure exerted by the elasticity of the expanded lung itself. Under these circumstances, although little diminution in the volume of the lungs (only that due to compression of their contained air) could take place, the intrathoracic vessels and the heart would be amenable to the effects of pressure, since the exit of blood forwards by the aorta would be free, and the outlet backwards from the right auricle into the cavæ would still remain open. The tricuspid valve, which is never fully competent in the normal condition (as tested after death), would allow, again, of some reflux into the right auricle, and so into the venous cistern. The point not so easy to determine, then, is whether the expiratory effort, with a full chest and closed airway, would compress the auricles and intrathoracic veins so as to empty them, as in Valsalva's experiment; or whether these would remain over-distended and embarrassed, as in Müller's. The first view is, probably, the correct one.<sup>1</sup> In either case an intrathoracic stasis would result; and as the forcible expulsion of blood from the veins of the limbs and trunk into the cavæ proceeded, the pressure within the cistern would continue to rise until it led to rending of the internal coats at some spot in its most capacious segment, viz., the inferior cava; and below the entrance of the hepatic veins. The cava, in fact, behind the liver is supported by the sides of the deep sulcus, or even canal, in which it lies; the second arrangement is well shown in Braune's fifteenth plate. This would tend to make the stretch below, the seat of highest distension; and this is where the obliteration has taken place.

<sup>1</sup>If the thorax is fixed in the expanded position, with the airway open, or only lightly closed, no effect on the pulse ensues as long as the expiratory effort is inhibited.

That the trauma arose below the entrance of the hepatic veins is shown not only by the patency of the latter, found after death, but by the total absence of ascites from the clinical symptoms. The safety of the auricles under over-distension in general may be, as Professor A. Keith (*loc. cit.*) has suggested, due to the support the pericardium would furnish when its capacity of reserve was overdrawn.

The possibility of such an injury having arisen, not from distension, but from mechanical strain acting *ab extra*, may be dismissed. The cava is nowhere tightly fixed to the spine; it is not included between the crura of the diaphragm, and as the diaphragm would be in some position of descent, no longitudinal stress arising from causes external to the vein can be assumed to have taken a part in producing the result.

Lastly, there arises a question whether, in Pollock's case, there was any predisposition to the occurrence of thrombosis—i.e., an exalted coagulability which would occasion thrombosis under conditions that would not otherwise have availed. This question is raised by the fact that one of the patient's brothers had previously died abroad with œdema of the lower part of the body which had been attributed to the pressure of a hypothetical sarcoma upon the inferior vena cava, and that another brother had died from embolism of the pulmonary artery, following thrombosis of the femoral vein. That there may be a familial condition which is the converse of the hæmophilic, one of exalted coagulability, is quite credible, but I cannot find that any such has as yet been observed in healthy individuals—i.e., a constant abnormal rapidity of coagulation in the shed blood, as distinguished from the variations which occur under well-recognized conditions in the same individual.

## Pathological Section.

March 18, 1913.

Dr. R. T. HEWLETT, President of the Section, in the Chair.

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### An Account of a *Bacillus* of an Unusual Kind isolated from a Case of Septicæmia.

By J. A. BRAXTON HICKS.

I AM bringing to your notice to-night an account of a case of a true septicæmia caused by an organism belonging to the saprophytic group of bacteria, and therefore not usually found as the cause of what is usually termed "septicæmia."

The clinical history of the case is most interesting, and is as follows: Mrs. A. S., aged 58, was admitted to the Westminster Hospital on August 21, 1911, under the care of Dr. Stanley Dodd, to whom I am greatly indebted for the clinical notes of the case. She was a widow of ten years' standing, had had five children and no miscarriages, the youngest child being aged 21, and the menopause had passed "some years ago." She complained that for the past eight months she had suffered from a vaginal discharge, at first merely the "whites," but latterly it had become blood-stained and offensive. On admission her temperature was 100·4° F., an offensive vaginal discharge was present, and bimanually, under an anæsthetic, the uterus was found to be enlarged and the external os patulous, while in the right pouch of Douglas was a "lump" about the size of a hen's egg. The uterus itself was explored, but nothing abnormal was found. After the operation the temperature still remained up, falling, however, almost to normal four days after the operation. On the seventh day after the operation the patient had a rigor and

the temperature rose to 105° F. The temperature continued to fluctuate between 99·5° and 105° F., with the occurrence of almost daily rigors, till the patient's death on September 15 (three weeks after admission). The patient's mental condition was peculiarly clear up till twenty-four hours before death, when a typhoid state supervened, and her physical condition was not that acute deterioration which not infrequently is the accompaniment of a septicæmia. During the last fortnight of her life I on two occasions withdrew 10 c.c. of blood from the right median basilic vein and isolated on both occasions the bacillus I shall later on describe.

A post-mortem examination was made by me on the body seven and a half hours after death, and the following conditions were found: The body was pale, still warm, and fairly nourished. There were numerous petechial hæmorrhages scattered over the abdomen. The uterine mucosa was in a condition of septic endometritis with hypertrophy and œdema of the muscular wall. The cervix was patulous and injected, while at the fundus uteri was a small submucous polypus. Several interstitial and subperitoneal fibroids were also present. In the right broad ligament was a cyst the size of a hen's egg, containing brownish, foul-smelling, purulent material. This cyst was adherent to the right lateral wall of the supravaginal cervix. The remains of the right ovary were flattened out over the cyst, but the tube itself was normal. The left tube, ovary, and broad ligament were normal. The inferior vena cava in its lower 4 in. and the upper part of the right iliac vein was full of firmish yellow clot (septic). Both lungs were full of septic infarctions, some of which were softening. The heart contained much clot, otherwise nothing noteworthy. Spleen large and soft, liver and kidneys yellow from toxæmia. No infarctions found other than those in the lungs.

The bacteriology of the case now alone remains to be described, for from the blood twice during life, and from the spleen and suppurating ovarian cyst after death, I isolated a bacillus identical in each case. The bacillus had the following characteristics:—

Morphology, &c.: The bacillus was a "coliform," Gram-negative, actively motile bacillus, growing well on all media and lasting well in sub-culture. Broth became cloudy and soon gave off an unpleasant odour. Agar-agar showed a white slimy growth in twenty-four hours, becoming yellowish and yellowish-brown later. Gelatine was slowly liquefied from above downwards. Milk clotted, with practically no acid formation in twenty-four hours, and in forty-eight hours the clot started to liquefy from above downwards, and subsequently became brownish.

Sugar litmus peptone: The reactions of these are somewhat variable even in successive sub-cultures. The most constant feature is the marked acidity, and gas production in glucose in forty-eight hours. In mannite, maltose, lactose there was, as a rule, a faint trace of acid formation and a bubble of gas. In sucrose the acid formation was rather more than in maltose, &c., but much less than in glucose, and only a bubble of gas was found. All cultures subsequently tended to become alkaline, though this was least marked in sucrose. All the cultures had an unpleasant odour. Potato showed a fawn-coloured growth in twenty-four hours, becoming darker later.

Pathogenicity: This was only tested on guinea-pigs, and fairly strong emulsions were found to be highly virulent for these animals, whether injected intraperitoneally or subcutaneously. The organism was recovered easily from the peritoneal fluid after death of the animal, the other appearances being those of septicæmia. Smaller doses were survived even when injected intraperitoneally.

*Conclusions.*—The bacillus just described belongs, I consider, to that group of bacteria known as the "*proteus* group," its growth in media, with production of a foul odour, its liquefaction of gelatine and milk clot, being the features relegating it to this group. It is pathogenic in largish doses to the guinea-pig and in the case recorded to a human being. It is this latter fact that has led me to consider this case worthy of record, for here is an organism which belongs to the group of saprophytic organisms causing a true septicæmia such as is usually associated with the parasitic bacteria, and, as far as I know, the organism is a new species.

## A New Spirochæta found in Human Blood.<sup>1</sup>

By HELEN CHAMBERS.<sup>2</sup>

(PRELIMINARY COMMUNICATION.)

### INTRODUCTION.

IN the course of a research on the pathology of Graves's disease a spirochæta has been found in human blood which, as far as I know, has not been previously described as infecting the blood-stream in man. Before discussing the organism in detail an explanation of the ideas which have led to its being detected is perhaps desirable.

At the Royal Free Hospital there are special facilities, in that there is a large supply of material for the study of the pathology of goitre, and during the last nine years the writer has examined over 500 specimens removed by surgical operation. The results of the early part of this work were published in the *British Medical Journal* of September 25, 1909. In this paper the conclusion was reached that, in some of the goitre cases, the thyroid gland shows changes which indicate a chronic inflammatory process, and it was pointed out that these inflammatory changes are similar to the effects produced in tissues by infection with the *Treponema pallidum*. In many of these goitre cases syphilis can be certainly excluded; many attempts were therefore made to find evidence of the presence of some other infecting agent in the thyroid gland, but without success. Now the majority of goitre specimens showing these histological changes were from patients who had suffered from the symptoms of hyperthyroidism—i.e., they were cases of primary or secondary Graves's disease. The inquiry therefore became concentrated more particularly on Graves's disease.

In many cases of primary Graves's disease, if the gland be examined carefully it is found that the changes are not uniform throughout the gland tissue. The absence of colloid and alteration in shape of the vesicles, with consequent opacity of the tissue, occurs sometimes in

<sup>1</sup> A Paper read at the Laboratory Meeting of the Section held at the Middlesex Hospital on May 20, 1913.

<sup>2</sup> From the Pathological Laboratory of the Royal Free Hospital.

localized areas. White nodules are found in the gland varying from the size of miliary tubercles to patches  $\frac{1}{2}$  in. in diameter and larger, and in the centre of these nodules it is common to find a collection of lymphocytes and plasma cells. This distribution and the recognition of the fact that vesicles similar in shape to those in Graves's disease are found in a thyroid gland inflamed as a result of injury, give support to the idea that the cause of the condition is an organism which has lodged in the centre of these foci.

A short time ago it occurred to the writer that, if this hypothesis be true, the infecting agent would probably not be limited to the thyroid gland. There might be a general blood infection, the thyroid gland changes and symptoms being due to local congestion or inflammatory changes caused by such infection—a somewhat parallel condition to what occurs in trypanosomiasis and sleeping sickness. In support of this theory it may be remembered that Graves's disease, like trypanosomiasis and syphilis, is usually associated with lymphocytosis and some swelling of the lymphatic glands.

The blood from several cases of Graves's disease was therefore examined, and a spirochæta was found, having in all the cases the same apparent characteristics. Further examination, with somewhat improved technique, has shown, however, that this organism is extremely common in human blood, and that it occurs in almost every specimen examined, in both patients and healthy people. Up to the present time the blood from twelve cases of Graves's disease, from twenty patients suffering from other diseases, and from fifteen healthy people has been examined—a total of forty-seven cases—and the organism has been detected in all except three. It has been found in children as well as in adults.

#### TECHNIQUE.

The blood is collected in a small Wright's tube and is allowed to clot at 37° C. for twenty minutes. The serum which has separated is then pipetted off. If a drop of this serum be placed on a slide and covered with a cover-glass  $\frac{7}{8}$  in. square and examined by dark ground illumination, in most cases one or two organisms can be found on the slide. The remainder of the clot is returned to the incubator, and after one and a half hours the serum which has separated owing to further shrinkage of the clot is examined by dark ground illumination. The organisms escape into the serum chiefly during the last stage of the



contraction of the clot, and by adopting the above procedure they are concentrated in a small volume of the serum. As a rule they are easily seen. The number found varies considerably. In the majority of specimens prepared in this way four or eight can be found on each slide, in other cases the organisms are very numerous, ten and more being found in each field of the microscope.

Some of the specimens of blood containing the largest numbers have been obtained from apparently healthy people. The number of organisms found fluctuates at different times. In three cases examined six weeks ago the blood contained the organism in large numbers; on many subsequent examinations comparatively few were found. They have now, however, increased and are almost as numerous as when the blood was first examined.

#### MORPHOLOGICAL CHARACTERS.

The organism is actively motile and is very variable both in length and thickness. The majority measure from  $4\mu$  to  $30\mu$  in length; very long forms are, however, met with. Some are extremely thin, like the *Treponema pallidum*, others are almost as thick as typhoid bacilli. The body is soft and flexible when thin and forms open curves, which are constantly being obliterated and re-formed. It is more rigid in the thicker forms. When free it moves in either direction. It is often attached by one end, sometimes by both ends, and the body then shows continuous lateral movements. In the thicker forms it shows a fine spiral structure, appearing as dark and light, closely set transverse lines—waves of motion passing longitudinally from end to end of the spirochaeta can often be detected. Sometimes the terminal portion moves from side to side independently of the rest of the organism. The ends are usually rounded, sometimes they are swollen and look like spores; in the finer spirochaetae the ends are tapering. The spirochaetae have been seen to vary in length, and are sometimes partly straight and partly spiral. Round spore-like bodies are sometimes found loosely attached to the ends or laterally on to the spirochaetae. Division takes place longitudinally and the organism has been seen in various stages of partial division. It differs from the *Treponema pallidum* in that the ends are usually rounded, the body is more flexible, and the curves are capable of straightening out. The thinner forms are, however, difficult to distinguish. Fig. 1 is a diagram of the organism as seen by dark ground illumination.

## STAINING.

The spirochæta has been stained with Leishman and Giemsa's stain. Small red chromatin granules are often found at the ends, and sometimes these granules occur along the length of the organism. The rest of the spirochæta stains faintly blue. It is not stained by Gram's method. The thick forms are easier to stain than the thin spirochætæ, and in stained films the latter are often not detected. The best results with stained films have been obtained from a forty-eight-hour broth culture. They were fixed in absolute alcohol for ten

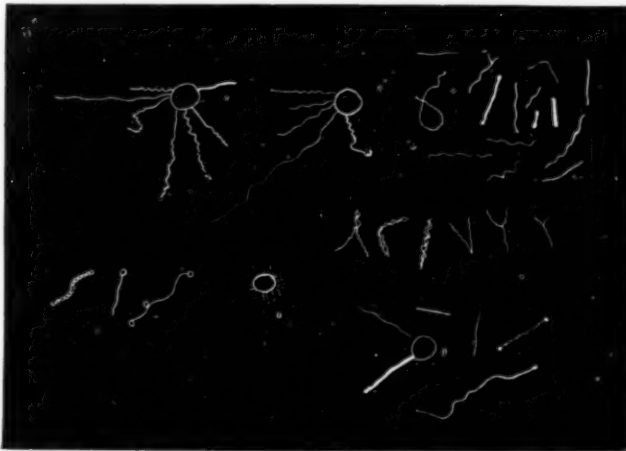


FIG. 1.

Diagrammatic representation of the spirochætæ seen in normal serum when examined by dark ground illumination.

minutes, then treated with 1 per cent. osmic acid for ten seconds and stained for ten minutes with aniline gentian violet. Fig. 2 shows photomicrographs of a film prepared in this way.

Many of the organisms are, when stained, almost straight; others show a very distinct spiral structure (*see fig. 2*).

Repeated, but unsuccessful, attempts have been made to stain the spirochætæ grown in serum which has been incubated for twenty-four hours. As will be seen later, this serum, on examination by dark ground illumination, contains actively motile organisms in large numbers.

## 140 Chambers: *New Spirochæta found in Human Blood*

The spirochætæ have been stained in blood-clot by Levaditi's pyridin method. The original method of Levaditi for staining the *Treponema pallidum* in tissue has not, however, given successful results.

### CULTIVATION.

If the serum which has separated from the clot after half an hour at 37° C. be pipetted off, left in the incubator at 37° C. overnight, and examined the next day, it is found that the clear supernatant fluid contains very few, if any, organisms. The fluid surrounding the corpuscular deposit at the bottom, however, contains the spirochætæ in very large numbers. They have obviously multiplied. They are, however, extremely thin and will not be seen at all unless a strong light is used for the dark ground illumination. If the serum be shaken and then vigorously centrifugalized and the supernatant clear fluid examined, it is found to contain numerous spirochætæ. Presumably, therefore, gravity has not much effect upon them when they are immersed in serum, and they are found in the corpuscular deposit because this is the only part of the fluid where the conditions are suitable for growth.

If blood be taken from a vein with the technique used for blood cultures, and introduced into broth flasks and incubated for twenty-four hours, the spirochætæ are found in large numbers amongst the corpuscles at the bottom, but not elsewhere—i.e., if the broth has not been disturbed. This occurs if  $\frac{1}{2}$  c.c. of blood is introduced into 40 c.c. of broth. The flask is shaken at the time the blood is collected and the culture medium is therefore largely broth. The spirochætæ disappear if the broth becomes extensively contaminated with other organisms. They have been found, however, actively motile for two days in conjunction with streptococci.

A broth tube containing these organisms was heated to 50° C. for an hour. They were still actively motile.

Blood has been shed into melted glucose agar tubes at 42° C. and the agar then allowed to set. The organisms multiply in the blood-clot and are found in large numbers twenty-four hours later, and are still actively motile after twenty days at 37° C. After several days' incubation, many thick forms are found in addition to the finer spirochætæ.

In all the above attempts at cultivation the organism has multiplied in the blood itself or in the first cultures taken. It has not, up to the present, been successfully sub-cultured on to artificial culture media.

*Pa. ha*

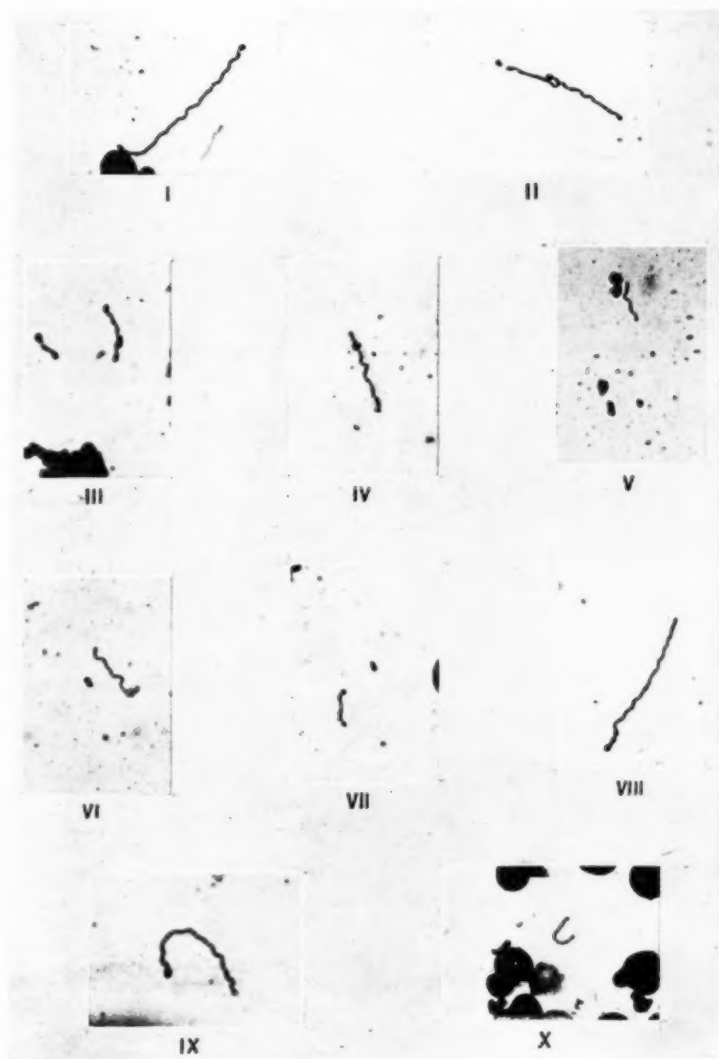


FIG. 2.

Photomicrographs of spirochaetæ from a forty-eight-hour broth culture of normal blood. Stained with aniline gentian violet. ( $\times 1,000$ .)

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CONCLUSIONS.

(1) A spirochæta has been found in human blood, and as far as can be said at present it is almost, if not quite, universal.

(2) It is probable that this organism is identical with some of the numerous forms of spirochætæ which occur on ulcerated lesions.

(3) The pathogenic effects of this organism, if any, have still to be determined.

I am indebted to Dr. Gertrude Gazdar for assisting me with this research.

PROCEEDINGS  
OF THE  
ROYAL SOCIETY OF MEDICINE

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VOLUME THE SIXTH

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COMPRISING THE REPORT OF THE PROCEEDINGS FOR THE  
SESSION 1912-13

SECTION OF PSYCHIATRY



LONDON  
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1913

## Section of Psychiatry.

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The Council think it right to state that the Society does not hold itself in any way responsible for the statements made or the views put forward in the various papers.

## Section of Psychiatry.

October 22, 1912.

SIR GEORGE H. SAVAGE, President of the Section, in the Chair.

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### PRESIDENTIAL ADDRESS.

GENTLEMEN,—I welcome you to this the first meeting of the first new Section of the Royal Society of Medicine. I have consented to give an inaugural address, somewhat against my feelings, for I believe that as this Section is one starting with the full intention of work for the advance of medical science, time might have been better occupied in learning definite results of original work than in hearing generalities. I have to admit that I have had very long and perhaps exceptional opportunities of observing mental disorders, and it may be of service to record some of my impressions and hopes. I will shortly outline the past, survey the present, and prospect the future.

Fifty years ago we were proud in thinking that we English were the great protectors of the insane. We introduced humane treatments and were content that the patients should be protected, while also society was safeguarded from injury.

A time of heaping up of statistics followed, but it was long before the true spirit of scientific investigation arose, and it is for this work that we are now labouring. No time has been without its earnest workers, and we have to remember that men like Bevan Lewis, Wigglesworth and others have done valuable work in large asylums in the North, and that Crichton-Browne encouraged men like Ferrier to combine general neurology with the investigation of mental symptoms. Many of us, too, have very grateful recollection of the bright and stimulating writings of Henry Maudsley, who, by endowing a hospital for mental diseases, is now doing his best to encourage original work. I cannot pass over Hack Tuke: he was one of the hardest workers I have ever met, and he had a power of taking from others the results of their work and reproducing it without bias or personal colour; I regret to find how little notice is now taken of his Psychological Dictionary, for in it are very many evidences that what seem to the younger men to be quite new and original observations or beliefs are neither new nor original.

Hack Tuke was a great recorder, and he has left a definite basis on which we may safely build. His Dictionary is a mine of wealth still worth working. With Hack Tuke, too, passed the historian of insanity. I cannot here refer to the many lesser lights that have during the past half-century served to illuminate limited tracks along the paths of progress, as I must curtail my retrospect.

Often advance is determined by some apparently trivial discovery, and in this way one cannot ignore the importance of the differential staining of the nerve tissues. When I consider the tens of thousands of sections of brain and cord which I made at Bethlem Hospital, using only carmine and logwood, I heave a sigh of regret at the lost opportunities.

The coarser anatomy of the nervous system, with the recognition of the localization of function, to which Ferrier added so much, was a starting point for more careful study of the intimate structure of the nervous system.

I am fond of the idea that we are yet, however, only like the London cab-driver, who has a most intimate knowledge of the roads and streets of the City, yet can know nothing of what is going on within the houses. It is certain that we shall know more of what is going on within, but I dare not believe that we shall ever fully understand what life and consciousness are.

Science must, after all, be limited by the restrictions of our senses. We are all governed by the organized inquisitiveness which we call science; we are collectors of facts, but we must avoid being mere fact-heapers, for in the multitude of mere facts not knowledge but confusion arises. Though immense numbers are not to be looked upon as certain bases to build upon, yet equally we must not be misled by the specious consideration of single interesting cases. The single swallow does not make a summer, but it may warn us of its coming; so the single case may direct our studies, but should not form at once the basis for a theory. As we move onward we must define our knowledge. As Sutton said long since, definitions are of use for one to rest upon while one is peering into the indefinite. The definite, as he said, had ceased to be alive. Death and the dead were definite. A definition should be the starting point for further investigation. Our special experience must make us alive to the danger of taking fancies for facts, and feelings for constant realities. Statistics we must have, but their value depends chiefly on the collectors. Mott has given us good examples of their value and importance. It takes long training to make a good judge, and we in England are very proud of our judges, yet in too many cases the medical observer is inclined to accept rapid one-sided observations, forming

a hasty judgment on a few facts. Let us be collectors and recorders, but at the same time let us recognize that what seems to us to be fixed and established to-day may in the future prove to have been only partially true.

It was only a few years since it was proved that no body heavier than air could ever be made to move under direction through space, yet now we have our aeroplanes which show that this idea was a mistaken one. It is in this way that I feel we must accept experimental psychology and psychic analysis. I still find leaders in medicine saying, What is their use? What have they added to medicine? We must not be always seeking for immediate results, we must be prepared to follow truth wherever it leads.

That related bodily nerve areas indicated visceral disease seemed so unlikely that Head's most valuable contribution to neural physiology stood a good chance of being regarded as incredible and useless, but now we value the observations and see in them further possibilities, making us still more impressed with the unity of the whole body and how one member cannot suffer alone. There may be blind alleys, but yet many of these will open later. Science cannot be limited by the apparently utilitarian views. I have seen one year the dropped boulder from a glacier a crude and useless mass, which in another year became transferred into a corner-stone of a house. A dislocated but firmly established fact may later be the keystone of the arch of progress, fitting in and supporting the whole structure.

And now as to our proper work. Probably we shall have to arrange for special sub-committees. It is certain that there must be a revising committee, whose duty will be to select for publication only such papers as seem to them to be of real value; sections for the material pathology will be necessary, and, on the other hand, there is need for special investigation of the psychical research and of hypnosis. These subjects cannot be ignored, but they require the utmost care in their consideration.

Some among us see in the inquiries of Freud danger of dwelling on the unhealthy side of our organic nature, but just as we use powerful and poisonous drugs in treating disease, so we may have to make use of means which, when ill judged, may be dangerous. There is always more danger directly we approach subjects which cannot be fully recognized by our senses. For all we know there may be some simple material basis for the various spiritualistic exhibitions, but at present we have to remember that we are very easily misled by our senses and that there is nothing more useful to mankind than prudent unbelief. Agnosticism in science is not infidelity, and we must cultivate it. We

must have the open mind, for after all the scientific man, notwithstanding his training, not infrequently is the most self-satisfied and unreasonable person with whom you may have to do. I have elsewhere spoken of the danger of self-satisfied science. During the past summer, lying on mountain slopes, yet unable to forget that I had a great responsibility arising from my presidential address, I thought of many things, and among them some wild imaginations took possession of me, and I said to myself that after all imagination has its uses. In fact, some great discoverers have thought that imagination is all important even in the most mechanical arts and sciences. Anyway, lying on a mountain slope I considered the address of Professor Schäfer on Life and its Origin, and I must say it left me still a believer in something more than the mere chemical theory as to its origin.

All the elements, however arranged, are not equivalent to any living thing. Truly the chemist has built up wonderful, so-called organic compounds, but they do not live. Tyndall was allowed in former years to propound the theory that life might have come from another planet, but that only shifted the weight from the elephant to the tortoise. I shall not be advancing knowledge, but I may start imagination, if I say I contemplated a universal force, call it vital ether, as yet unrecognized and possibly beyond human powers to recognize, which, like the astronomers' ether, is universal and prevalent, this acting on what are called living bodies according to their structure. In the vegetable work the machinery, the receiver, is limited in its powers, while in the developing scale of animals the vital ether is more and more in deep relationship with the organism. As long as the organism can receive this vital force it lives; when this power is lost the body becomes the mere clod. The consideration of this theory caused me much pleasure, but I admit it has no ground of fact, though it represents, perhaps, in a crude way all we know of life. It is nearly related, I recognize, to other views both metaphysical and theological.

I thought of the captain of a ship who is constantly casting his searchlight into the darkness ahead of him that he may direct his course and avoid danger. So let imagination be as a searchlight, intermittent but penetrating. We must then be prepared to make experiment and trials even in what may appear unfavourable conditions, and we must be always ready to recognize our failures and be willing to try back. It is, however, rather saddening to see a distinguished man following some will o' the wisp though his friends may warn him of his error. Yet these may be beacon-light warnings. We may learn as much from our errors as from our successes.

As I have said, we must be diligent in collecting and recording, then will follow the classifying or arranging. In some cases naming is necessary—it is the evidence of advance, and has the value and danger of definition. A great danger arises from the too ready naming of groups of symptoms, as if they were entities. A traveller in a new land often gives names to honour men who have discovered or who have attained a world-wide celebrity, and some doctors are inclined to give names of men to disordered bodily states. I think this is a mistake. Let our naming be more natural and have some relation to the pathology. When one sees the endless names given to disorders depending really on some central sensory disorder, one is either amused or disgusted. But it must be admitted that we Englishmen might be jealous if the name of our distinguished countryman Hughlings Jackson were disregarded in relation to epilepsy.

Hitherto, the two subjects of neurology and mental disorder have been separated, but with the more exact knowledge of the nervous system as a whole the distinction has become lessened, and neurology has claimed a very direct interest in mental diseases. This is doubtless an advantage from some points of view, but for those of us who have gone through a long training among the insane, it seems that the future neurologist needs such a section as this to give him help in understanding the working of the mind in disorder. The neurologist, following to some extent the lay public, looks upon asylum treatment as the very last to be followed, and even the alienist is forced by public opinion to fall in with plans which after all he believes to be only the second best. The prejudice against asylums may be said to be organic, but the dawn is near, and the mental hospitals and retreats will carry on the excellent work which our asylums have done and are now doing.

We here hope to study the nervous system as a whole. I have often quoted what Sir W. Gull said to me when I first went to Bethlem: "The brain is like a wealthy gentlemen with many servants, and he may be badly served by any one of them." The brain is like the belly and its members and cannot suffer apart; and this is one of the most difficult lessons to learn and to teach—that though the mind may in many ways be apparently healthy, and though many of the reactions to the environment may be normal, yet the brain and the mind may be disordered. Almost daily I hear friends say that surely I cannot consider their relation mad for that he answers perfectly rationally when they talk to him on general or social subjects. There are only a limited number of ways in which the nervous system can express itself, and therefore similar symptoms will be



present whether the central nervous system is primarily affected or whether its functions are interfered with by the misconduct of one of its servants. It must also be never forgotten that so-called mental disorder is gauged in relationship to conduct and that certain disorders depend more on the surroundings of the patient than on the patient himself. I have long been in the habit of referring to the social misfits which depend on the surrounding rather than on the patient. Social and mental disorders are nearly related, and one of our most difficult problems is to decide where the badness ends and madness begins. And here once more would I maintain that there are many mental disorders which deserve the name functional in so far that they are not represented by any material change in the central nervous tissues. Nature provides the iron but man makes the horse-shoe for service.

I have elsewhere written on morbid mental growths, and it is among such growths that we meet with some of the most intractable mental disorders. That the mean man should become with age a miser or that the cunning youth should become a thief is not surprising; yet I do not expect ever to find any special changes in the brain representing meanness or acquisitiveness. I recognize that want of something in the nervous workshop may cause loss of control so that the person is no longer able to accommodate himself to his special surrounding, but this alone will have to be measured by means which at present are not available. The bodily and mental relationships are very difficult to follow—take as an example what have been looked upon as alternations of neuroses. I recall the case of a young woman who was admitted into Bethlem Hospital, suffering from acute mania. This state of excitement lasted for some weeks, when suddenly she became sane but paraplegic. The paralysed state lasted for a time, to be replaced by a period of mania. It has long been recognized that if certain patients with glycosuria become insane the sugar disappears from the urine. Hay asthma may be absent during a period of mental disorder, and only recently I met with a very rare condition in which migraine passing off at middle life was replaced by definite mental disorder. These are perhaps more readily understood than the relief of mental disorder by some form of physical illness, and I am inclined to think that the scourging of the lunatic in times past might have occasionally been a help to recovery. There is certainly no doubt that in the skin we have a vast distribution of nervous tissues which may be appealed to in treatment.

It is difficult to trace the relationship between bodily cause and mental effect in such a case as this: A young officer suffered from a fall

on his head and was sent home in a state of profound stupor. There was no power to rouse him. Skiagrams being taken, there was apparently some thickening over the vertex. I may here say this was not found to exist. He was placed under an anæsthetic and a piece of bone removed. On recovering from the operation he was perfectly sane and remained so for a long time. I believe later he had some relapse, but I saw him for some time after the operation and he was sane in every way. We found no indication of any local lesion. Such experience makes one think deeply.

Waves of thought roll on and leave shore-lines and raised beaches. Most of us here have watched the tide of evolutionary thought as represented by Darwin, Herbert Spencer and Wallace rise, and though there have been some ebbs and flows yet the advance has been fairly steady and has left a shore which will never be obliterated. Weismann and Mendel are now beating on the coast of the indefinite and they have still to establish their lines or fall back, leaving rounded pebbles of thought which may serve for future building. It is certain that one of the most important parts, not only of our special work but of the world's work, is the true consideration of heredity and its far-reaching influence. That much is transmitted from parent to child is admitted, the existence of "species" is sufficient evidence of this, the persistence of type under varying conditions. I am one who cannot accept the belief that nothing acquired by a parent can be passed on to the child. In simple things such as handwriting I see direct transmission of habit. Probably the students of neurology and psychiatry are more impressed than the students in many other branches of medicine by the very clear evidence of the passing on of nervous disorders from generation to generation. Just as it is clear that many of the most fixed racial and specific characters are transmitted, so it is equally clear that some very marked nervous abnormalities are similarly transmitted; but it is also clear that the limit of transmissibility is not known, for I am of the opinion that just as genius is rarely produced in the succeeding generations, so there are many of the nervous and mental disorders that, like genius, are not transmitted.

The general result of all recent investigation points to the occurrence of characteristics in children which were not present in the parents, but did occur in grandparents, or in collateral branches. It struck me as an interesting suggestion that some of these masked inheritances might be uncovered during dream states, and that amusing essayist Horace Hutchinson even suggested that the dreams of flying which are common are reminiscent of the arboreal existence of our simian

ancestors. But, joking apart, that there may in dream memories be some ancestral and inherited memory seems possible.

I wish now rather to develop the question of heredity, though I have nothing novel to add to the splendid work done in our Section by Mott. This work is growing and its results will live. We have got so far as to disregard the older faith that there was a distinct evidence of passing on of disease as such. We now are content to say that a tendency is transmitted, that a soil is provided, and that other environmental conditions are the true exciting causes of disease. The special, or, I might say, the specific tendency to develop particular disordered states varies so that those prone to neuroses are not necessarily more liable to febrile and other diseases, though I have been very much struck with the tendency of members of certain neurotic families to contract any febrile disease which may be prevalent. It used to be thought that the nervously weak and unstable were unusually likely to take phthisis, and the death returns from idiot asylums and similar institutions seemed to strengthen this belief. Certain of these families seemed as if they had lost the immunity which to a great extent saved the dwellers in cities and in populated places. They seemed to revert to the condition of those groups of isolated people which are met with in the islands of the West, who contract and suffer severely from every epidemic disease which is introduced. I do not believe in the transmission of any definite form of mental disorder, but I have met with instances in which both parent and child have had similar delusions, such, for instance, as that they had committed the unpardonable sin. In such cases similar education and surroundings occurring in the persons of a like temperament led quite naturally to similar delusions. We accept the inheritance of bodily likeness and of the material bases of thought and feeling, likeness in the senses and their reaction to surroundings, and it is therefore not surprising to find a tendency to inheritance of certain disorders of mind in which sensory troubles are most marked and potent in producing morbid conduct. It is almost universal in my experience to find the sufferers from organized delusional insanity to belong to insane and highly unstable nervous stock. The tendency to morbid habit, as seen in recurrent insanity, is also constantly associated with neurotic heredity. It is now almost universally recognized that long life is a family tendency, and parallel to this there is the predisposition to decay along certain lines; thus it is not uncommon to meet with families in which the arteries become diseased with age; and mental senility in one of its many forms may recur in each generation. I recall one well-known and distinguished family the

members of which all lived to advanced ages, but they all presented similar evidences of decay by failing in the brains first.

My opinion, then, is that there is no doubt that in certain cases there is transmitted a tendency to nervous or to mental disorder, but that only a certain proportion of cases in asylums can be proved to have had insane relations.

I have been interested to find that recent statistics bear out what was my experience, that at least one-third of all the patients admitted into asylums have insane blood relations. A very important point which Mott has brought out more clearly has long impressed me. It is that if the neurosis is to be transmitted it probably occurs in the offspring at an earlier age than it did in the parent. This is a very practical question, for when consulted, as I constantly am, as to the future of the children of insane parentage, particularly as to marriage, I always ask as to the age at which the insanity in the parent first came on, and the age of the child about whose future I am consulted, and I always oppose any marriage till the child has reached maturity, which I place at 25 years of age. This is only a provisional rule, but one must have some rule to go by. The danger to the offspring of insane parentage depends, too, to some extent on the proximity of the parental insanity to the begetting or birth of the child. I have known perfectly healthy children born some years before an attack of insanity to be followed by neurotic children born after the insanity of the parent, and, what is more, I have known healthy children born before an attack of insanity, while children born near the time of the attack have been unstable or weak-minded, and I have known, after a healthy interval of some years, healthy children again to be born. What was transmitted or what was withheld is unknown.

In considering heredity, too much stress must not be laid on the existence of some forms of mental disorder in the family. As I have already said, insanity, like genius, may be an accident. It is certain that some families in which every form of neurosis has been represented have succeeded in breeding out of the tendency. I recall one instance in which various forms of mental disorder were present in one generation but in the next, by suitable mating, nothing really morbid was seen. It was interesting to see in some members of such a family eccentricities or tricks of manner appearing, so that I have seen insanity in one generation followed by musical or other aptitude in the next, while in the third generation, or in some members of the second family beside the normal members, were some with tricks such as the facility, untrained, of mirror writing. We must not believe too much in what

has been well called the tyranny of the organism. That conditions have very much to do with the production of attacks of insanity I have no doubt. One of my favourite similes in teaching on the question of heredity was to compare it with the mycelium of the mushroom. This spreads far and wide, and is not recognized till suitable conditions lead to what we call the mushroom which comes to the surface. So the neurotic inheritance spreads far and wide and is deeply seated, but the occasion for its development may be wanting.

I cannot pass over the very important question (which runs some danger of becoming popular) of the position of the defectives and our duty to them. Several of you attended the Congress of Eugenics, and there was no doubt about the earnestness with which the subject was considered. In this congress the question of the transmission of mental weakness was very fully considered, and while I am as convinced as anyone can be that in many cases the feeble-minded tend to reproduce the defectives, yet some of the members of the congress would include almost everything which was eccentric, and genius and folly, therefore, would both be isolated by them. The principles of eugenics must appeal to us all, but we must not forget what Professor James so forcibly pointed out, that attraction means something different when referring to the magnet and steel filings than when Romeo and Juliet are concerned. In the latter instance the attraction is not a mechanical compulsion.

We have to look upon the defectives as being human and being very near most of us; there is no specific difference, only variation. And it is therefore not hard to explain why they tend to reproduce their like. It is fully recognized that it is rarely that great peculiarities in a parent are transmitted, but the slighter ones are. The social defective or the weakling with want of control is parallel to undeveloped man. This fact of the similarity of offspring to parent in defectives must have great weight in our treatment of such persons. Some, like many savages, can be trained but hardly educated.

Before leaving the subject of heredity, having expressed my opinion and given my experience, I am still in great difficulty as to what may be transmitted and what can be explained as simple reaction to surroundings of a mere mechanical nature. Reflex arrangements are established and passed on, and it is certain that whether we consider instincts as survivals of past acquirements or stages of the evolutionary process, they are passed on in the most complicated way. That a young water-fowl should be able to swim within a few minutes of emerging from its egg (and this I have seen) is comprehensible, but that a beetle

or a butterfly should do what other beetles or butterflies have done, though they have no immediate parentage, is difficult to follow. I may give examples. In one case a medical friend interested in entomology had some eggs of a rare moth which he hatched in cases, and the caterpillars in due course passed into the stage of pupa; in one of the cases the branches of a tree had been placed for their accommodation and the pupa resembled in colour the bark of the tree. In another case there were bamboo sticks and the pupæ in that case resembled in colour the bamboo. This certainly looks like a simple reflex power of adaptation, but what can one say of the following:<sup>1</sup> The Yucca moth emerges from its chrysalis case just when the large flowers of the Yucca open, each only for a single night. From the pollen of one of these flowers the moth collects and kneads a little pellet which she holds beneath her head with enlarged bristly palps. Thus laden, she flies off to another open flower. She pierces with her ovipositor the tissue of the pistil, lays her eggs among the ovules, then darting to the top of the pistil she stuffs the fertilizing pollen into the stigma. It has been proved that unless this moth visits the Yucca there are no ripened seeds. The grub consumes about one-fifth of the fertilized seeds, leaving abundance for the future of the plants. This process has been slowly evolved; one hardly dare in time compute the ages which must have passed in the production of this perfect arrangement. Something has been transmitted, we have to admit, or else you must accept a still more difficult solution—that each of the independent acts is a mechanical reflex to its surroundings. If, then, we accept such possible hereditary transmission, I think we must be very careful in dogmatizing on what may be reproduced in the offspring from the parents.

Next to heredity alcohol has been looked upon as a potent cause of insanity, and there is no doubt that a good many patients are yearly admitted to asylums in whom excess has played a part in producing the disorder; but, again referring to Mott's work, there can be now no longer any doubt that certain people suffer in the viscera while others suffer in their heads. It is interesting to note that in the recently published report of the Irish Commissioners in Lunacy they say the general conclusion of their investigations is that alcohol possesses comparatively small importance as a cause of insanity in Ireland.

I have referred to the waves of thought and their remains or effects. Now we are on what might be called the chemical wave. Cells have

<sup>1</sup> Kerner's "Natural History of Plants."



played their part, and bacteria are having a distinguished career, but the results of cells and bacteria are, after all, supposed to be chemical products.

I admit that the whole matter of blood and its various possible constituents is too much for me. I recall the happier days when working among the earliest of his pupils with Professor Klein some four or five constituents were allowed to the blood. Now, as on every hand we have theoretical additions, I have to exercise a faith in them, while I ask *you* to extend faith and imagination along other lines. Thus, dreaming on mountain slopes, I wondered what the internal secretion of the brain might be. The discoveries on the potency of these secretions are very striking. It appears as if every organ had a twofold relationship. First with the greater world, second with the smaller one of self. The central nervous system and its nerves are in wide relationship with the outer world, and yet there is the undefined and not understood Consciousness which may be the result of the internal secretion. It pleased me to think of feeling and consciousness as the by-products of nervous action, and I could not help seeing in some instances of morbid mental states evidence that the idea was not altogether wild.

One of the dangers of the present time is that in consequence of physical discoveries, what have been looked upon as certainties no longer hold that position. I have already spoken incidentally of this, but now I have to say that what twenty years ago or less would have been laughed at is accepted as at least worthy of study. Though telepathy and spiritualism are outside our province, unless they are considered from the morbid side, yet hypnotism and suggestion and psychical analysis have taken very important positions, and are doubtless associated with the rapidly developing science of experimental psychology. We find in the last, the comparatively new science, most attractive work, and though I find the physician of to-day prone to ask, *cui bono?* I can only reply, we must "wait and see"; that we are prepared to follow truth where it leads, and that a dim light is better than none in such darkness as the realms of life and consciousness.

And now, Gentlemen, having rambled over a very wide field, I feel that I must leave it for you to cultivate. It is not forest or virgin soil, but it is productive, and earnest work will have its reward.

In concluding I would say that, like Moses, I view a land of promise which I shall not live long enough to enter, yet, like him, I watch the battle, and as when Moses's hands were supported by Aaron and Hur, Israel prevailed, so I feel that, supported by my two Vice-Presidents, my feeble efforts will be certain of some success.



## Section of Psychiatry.

December 10, 1912.<sup>1</sup>

Dr. PERCY SMITH, Vice-President of the Section, in the Chair.

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### Case of Presbyophrenia (Alzheimer's Disease).

By W. H. B. STODDART, M.D.

M. A. B., FEMALE, married, aged 68, of sober habits. Admitted October 31, 1912. No physical signs except those of senility. Sensation and perception normal, no hallucinations and no apraxia. Profound amnesia, disorientation and confabulation.

At the meeting the patient stated that she had been in the hospital only a few hours, had just come over from the Isle of Wight, and that her son had just had an accident while skating, which statements were all absolutely untrue. No symptoms of neuritis.

### DISCUSSION.

Dr. STODDART added that the patient exhibited the condition of presbyophrenia as originally described by Wernicke and Kahlbaum—viz., amnesia with confabulation, illusions of memory and recognition, and disorientation. The amnesia was said to be allopsychic not autopsychic, in other words, the patient could remember fairly well what happened to herself but not what happened to others. He had been asked if there was a history of alcohol in the case, as it was similar to the polyneuritic psychosis; but alcohol was denied in all the documents supplied, and also in the history given. She was said to have been always quite temperate in her habits.

<sup>1</sup> Clinical Meeting at Bethlem Royal Hospital.

Dr. BERNARD HART asked if there was any diagnostic difference between presbyophrenia and polyneuritic psychosis other than the history of alcohol.

Dr. STODDART, in reply, said that there seemed to be no difference between the two conditions, except that presbyophrenia seemed to come on at a later stage of life. Microscopical examination of the nervous system in such cases was said to have revealed multiple plaques of sclerosis in the cerebral cortex. But that had been denied as being characteristic of this disease, and they were due simply to old age.

### Case for Diagnosis.

By W. H. B. STODDART, M.D.

T. R., MALE, aged 59, mining agent. Admitted\* September, 1905. Family history negative. Eighteen years ago fell from a tramcar on to his head and had attacks of petit mal eight months afterwards. These occurred about once a year. Later had nocturnal convulsions. No fits since 1902.

Three months previous to admission had an attack of dysentery on the West Coast of Africa, was invalided home, and was cured at the Dreadnought Hospital. Six weeks previous to admission he wrote a perfectly sane letter to his wife, but has not written since except from dictation.

There is no disturbance of sensation. The patient stands in a peculiarly rigid attitude with shoulders raised, and walks with short steps without bending the knees. He knows what is going on around him, but does not know where he is, and suffers from profound loss of memory. He does not know which is his bedroom, although he has occupied the same for the past seven years. Well-marked Witzelsucht. Pretends to be dangerous but never does any harm. Jokes about his symptoms and exaggerates them. Shows Romberg's sign, but this is probably a joke on his part. Fabrication at times.

### DISCUSSION.

Dr. S. A. K. WILSON remarked that in estimating the comparative localizing value of Witzelsucht in such a case as this, one required to know whether the Witzelsucht was pathological, or whether it was not really part of the patient's character, which might have been present before the illness. He therefore

asked at what date the symptom was noticed. He was struck by the fact that in this patient it never ceased, whereas in most of the cases in which he had seen Witzelsucht in association with organic brain disease, for instance, in frontal tumour cases, one would not say it was absolutely constant. He had seen it also in temporal tumour cases. He therefore questioned whether, in this patient, one could place any localizing value upon it. Here there was a definite history of a fall, and of petit mal and nocturnal convulsions, and there might have been a focus of disease commencing somewhere on the front of the head, from which the degenerative condition might have started. He asked if the patient had anosmia or parosmia, or any olfactory hallucinations. Part of the rigid and stereotyped attitude in walking he regarded as a psychomotor disturbance, and considered that it might be associated with disturbance of part of the function of the intermediate precentral portion of the frontal lobes.

Dr. STODDART, in reply to Dr. Seymour Tuke, said the condition of the patient on admission was the same as now. He had had the advantage of a talk with the patient's son, who was a medical man of standing, and he told him that his father did not exhibit either Witzelsucht or the curious motor phenomena before his illness. His sense of smell was normal, and he had never suffered from olfactory hallucinations. The disks and sight were normal.

### **Œdema of the Thighs in a Katatoniac.**

By W. H. B. STODDART, M.D.

THE patient adopts a persistent kneeling attitude. This case was shown to raise the question whether posture alone is sufficient to cause œdema.

#### **DISCUSSION.**

Dr. STODDART added that the patient spent all his time on his knees. He came in a state of acute confusion, loss of memory, disorientation, hallucinations, anaesthesia, and he gradually lapsed into this curious stuporose condition. The knees at one time got sore, and since then they had been padded. The posture in itself was not sufficient to cause such œdema, because clerks who sat in one posture with the legs dependent for hours daily did not have it. This patient slept well at night for about six hours, and perhaps for an hour or so in the afternoon. He had asked Dr. Gordon Ward to examine the blood for him, and Dr. Ward would say what he had found.

## 16 Stoddart: *Presenile Katatonia (? Dementia Præcox)*

Dr. GORDON WARD said that examination of the blood revealed nothing of great importance. There was some diminution of red corpuscles, without corresponding reduction of hæmoglobin, and this suggested that the blood might be merely diluted, rather than that it was true anæmia. This seemed to have a bearing on the presence of the œdema. The white corpuscles were about 6,000, and there was some lymphocytosis. Such had been reported in a good many cases of hereditary œdema and the familial forms of œdema. He had not been able to estimate the total blood volume.

Dr. R. H. COLE said this attitude was not peculiar to katatonia (dementia præcox). He had under care what was considered a case of maniacal-depressive insanity in a young man, who, four times a day for two hours, was on his knees muttering silently, as this patient was, and whose conduct was normal at other times. But there was no œdema about his extremities, which he regarded as due to the blood-pressure being very low and to weakness of the heart's action in the case exhibited.

Dr. J. G. SOUTAR said that in cases of this kind localized œdema was not infrequent. It was found in different parts of the body and it was often necessary to keep patients in bed to get rid of it. The poor circulation—the low blood-pressure which was so commonly found in these cases along with the maintenance of unnatural attitudes—seemed to be enough to account for the œdema.

Dr. STODDART added that it was not uncommon to see œdema of the feet and hands in stuporous cases in association with a sluggish circulation.

### **Presenile Katatonia (? Dementia Præcox).**

By W. H. B. STODDART, M.D.

E. W., FEMALE, married, aged 61. The only suggestion of inheritance is that a sister attempted suicide by cutting her throat. Three weeks before admission she found some moths in her clothing, became worried, and developed delusions that her house was filthy and that she had no respectable clothes. Verbigeration developed with stereotypy, negativism and universal rigidity. Well orientated on admission, but rather more confused now. Memory fairly good.

Dr. Stoddart contended that it was irrational to call this grouping of symptoms "dementia præcox" at one time of life and to give it another name when the patient was advanced in years.

DISCUSSION.

Dr. SEYMOUR TUKE said that cases like this sometimes suddenly recovered. He mentioned a case of sudden recovery with lasting results occurring under his own care about twenty years ago.

The CHAIRMAN (Dr. Percy Smith) said this was the kind of case which under the old nomenclature would have been called "agitated melancholia in a person approaching senility"; and, as Dr. Seymour Tuke said, one would not say there was no hope of recovery. Directly a case was labelled dementia, especially in a person who was somewhat old, one felt that the prognosis was bad. He gathered that this patient's memory was fairly good, and where that was so in melancholia the prognosis was not absolutely bad. Agitated melancholia in a person approaching old age was more serious than in a young person with mental depression. Verbigeration, stereotypy, negativism, and rigidity, formed a group of symptoms which one saw in dementia præcox, but it was scarcely "præcox" in this case, owing to the patient's age.

Sir GEORGE SAVAGE said the words "agitated melancholia" passed through his mind when he saw the case, and he also would be reluctant to pronounce such a case as hopeless. It was the type of case which he regarded as very active mental pain, which might, if the memory was not much affected, persist for years. In this, as in bodily suffering, perhaps the best thing was to give opium. There seemed to be no symptoms of real dementia here.

Dr. SOUTAR said this was a type of case which caused one to wonder whether there were definite mental diseases which could be grouped in this way. Were these symptoms absolutely confined to cases of dementia præcox? As had already been pointed out, in this case the great feature was the agitation and distress, which seemed to have originated in an obsession. She imagined that she found a moth in her clothes, and this idea was followed by more organized delusions. That did not seem to be a prominent symptom of the cases which were spoken of as dementia præcox, and it was extending the notion of dementia præcox too far to include such cases as this merely because such symptoms as stereotypy and negativism occurred amongst the indications of mental disorder.

Dr. STODDART, in reply, said he considered that the prognosis of this case was not hopeful. The other comments would take too long to answer. The patient did not present the usual symptoms of melancholia, but he had been pleased to hear such expressions of opinion; one of the ideas in the formation of this Section being that speakers should freely give their views and invite criticism.

**Senile Dementia with Apraxia.**

By J. G. PORTER PHILLIPS, M.D.

H. T., MALE, aged 65. Admitted December, 1906. A few months previous to admission became silent and depressed, could not concentrate his mind on business, and became dazed in the morning. Had some glycosuria on admission. At times perfectly clear mentally, at other times, especially after smoking, exhibits verbigeration, stereotypy, and apraxia with ideational inertia.

**DISCUSSION.**

Dr. PHILLIPS added that the chief persistent symptom from which the patient had suffered was insomnia, but he could now sleep without the aid of a draught; in fact, great improvement had occurred since the notes were written. The attacks often started after smoking, or after some excitement.

The CHAIRMAN believed smoking might have an influence in determining the attacks. Tobacco seemed to interfere with the flow of ideas in some people; and in his own case he noticed that he was not as good as usual at golf after he had been smoking.

**Maniacal-depressive Insanity (resembling General Paralysis).**

By J. G. PORTER PHILLIPS, M.D.

E. H., MARRIED, female, aged 59. Admitted June 19, 1912. One sister insane. Previous attacks 1894, 1896, and 1907. On this and last occasion knee-jerks almost absent. Sensation, perception, and memory normal. Excited, talkative and incoherent, with excessive large-joint movements. Delusions of exaltation. Cerebrospinal fluid: Positive Noguchi, negative Nonne-Apelt. Very slight lymphocytosis, a few plasma cells. Wassermann negative. Conversation still somewhat bizarre, but patient appears to be improving.

Dr. PHILLIPS added that the patient was now nearly convalescent. She had had very little treatment. After the birth of her last child twenty-one years ago she developed iritis, since when inequality of pupils with no reaction to light had persisted. The question arose as to whether it was

general paralysis. When she entered the hospital she was wildly excited, had delusions of grandeur, tremors of tongue, lips and hands, with nearly absent knee-jerks. Her memory was fairly clear, and perception and orientation fairly good. There was no intracranial pressure or tumour, no headache, vomiting, or convulsions. No specific history was obtainable. Although it was purely maniacal-depressive insanity, it might have been mistaken for a case of general paralysis, especially when she was in the excited condition. A support to the diagnosis was derived from the fact that she had had previous attacks, from which she recovered.

### **Acute Confusion in a Child, aged 12.**

By RALPH BROWN, M.B.

A. F. B., FEMALE, aged 12. Admitted June 22, 1912. Mother had some psychosis just before birth of child.

The patient was born in Egypt, and while there had an illness at 18 months, with headache, fever, vomiting and thirst. These attacks occurred about every three months at first, but gradually became less frequent; now about once a year. No doctors ever diagnosed the condition. Enteritis at Suez at 2 years of age. Operation for adenoids three years ago. Urine 1019, no albumin or sugar, indican plus, oxalates, pus cells, bacilli, no casts. Cerebrospinal fluid normal. Leucocytosis reached 17,000 a few weeks after admission. Eyes normal. Choreiform movements of the arms on admission, with hyperæsthesia of the skin of the abdomen. Patient was confused, disorientated, incoherent, and dirty in her habits. Persistently chewed the bedclothes. On July 22 temperature rose to 100° F., and dropped in the evening to 96° F., after which she did not speak until the beginning of September. Tube-fed. Appears to be improving.

### **DISCUSSION.**

Dr. BROWN added that of late the attacks had become less frequent. The heart sounds were muffled. Examination had been very difficult owing to the constant movements of the patient. At times a systolic bruit could be detected. There seemed to have been no anæsthesia and no hallucinations. There had been some hyperæsthesia of the abdomen, but that soon passed off. For a time it was thought the condition was hysterical chorea. She had had "growing pains" a year before admission. Was it imbecility, of late



development, due to syphilis? Probably not, as the Wassermann reaction was negative and the child's condition showed considerable improvement under treatment. He considered that there was a choreic element in the case and that the correct diagnosis was "acute confusional insanity due to a toxæmia."

Dr. F. E. BATTEN said that these cases of so-called chorea in children had interested him a good deal: and he had seen two cases in children, aged between 2 and 3, with a curious mental condition, including loss of speech, and most violent movements, exactly like those of chorea, though obviously not of rheumatic nature. He had watched those cases in hospital for six months, during which time the movements continued, and the mental condition remained the same, then gradual and steady improvement took place, but not complete recovery of intellectual faculties so far as his cases were concerned, though he had watched them now for five or six years. He had never had the opportunity of examining such a case post mortem. According to the parent's statement, these two children were quite normal before the onset of illness. One of the cases had still considerable mental defect. They were not due to meningitis, for no change could be found in the cerebrospinal fluid. He had been unable to find out what was the cause of the condition. The number of white cells in the blood mentioned by Dr. Brown—viz., 17,000 per cubic millimetre—did not necessarily indicate a leucocytosis in a child; anything up to 20,000 might be regarded as normal in young children. In reply to the Chairman, Dr. Batten said one of the children was the daughter of a soldier, but there was no evidence of syphilis in the child; he did not test the father. Other members of the family appeared to be normal. Insanity in the collaterals was not inquired into; this was unfortunately not done as often as it should be.

Dr. J. F. BRISCOE thought a likely suggestion was that the child was suffering from a contributory cause of auto-intoxication, for the motions were very offensive. The child had been apparently overtaxed by education, and he had procured a specimen of her handwriting, which he showed; and she was able to play the piano. It would be interesting to see what effect a continuous rest-cure would have upon her, especially if it were prolonged at Bethlem Royal Hospital for the insane. There was no evidence of scars; the teeth were correct; and there were no nodes nor a ground-glass appearance of the corneæ. But was this confirmatory that there has been no specific intoxication in the breeding of this child? There was probably a nervous taint, and the breakdown had been excited by excessive mental strain. She was highly sensitive, for she kept her head down when addressed, although with persuasive conversation she could become interested, since she smiled and talked; and without any effort, from dictation, she wrote a very clear letter in his presence, correct in lettering, spelling, and stopping. Here was a good instance of a child in which he thought heredity and stress emphasized the importance of the problem of studying the mental and physical condition of children when the time for their education was to be commenced. There

was no evidence that the sexual system had as yet unravelled itself, since the mental nurse in attendance said "she has not seen any menstrual flow, but that the child has been very dirty in her habits."

Dr. SHUTTLEWORTH asked whether in the former attacks of headache, fever, vomiting, and thirst, there were mental symptoms similar to those recently observed. Or were there choreic movements associated with those attacks? Also, in the intervals between her illnesses, was she subjected to the pressure of ordinary school life? And had there been any symptom pointing to the near advent of the menses, which sometimes occurred early in girls of oriental birth?

Dr. S. A. K. WILSON said he did not doubt that this was a toxi-infective condition, but possibly the origin might be of a very specific nature, meaning thereby not syphilitic. He was specially mindful of the involuntary movements of the nature of tremor and chorea; and not all toxic cases showed such movements. It was possible that in this case the causal poison emanated from the liver; there was a group of liver conditions in which involuntary movements were seen and in which the mentality was sometimes affected. A combination of mental symptoms with involuntary movements and obvious somatic symptoms was not infrequently met with. These poisons originating in the liver seemed to have a specific action on the basal ganglia, though other parts of the cerebrum might be affected. He did not know of any means of testing the liver function in conditions of this kind. He asked whether the patient had ever had icterus, or anything pointing to liver deficiency. If this case were carefully followed up it might prove of help in corroborating the work which had been done recently on the subject in this country and on the Continent.

Dr. GORDON WARD did not find himself in agreement with the remark of Dr. Batten that 17,000 leucocytes was not leucocytosis in a child, especially as here there was also iodophilia. There was a toxic factor in the case, though what it was he did not know. With regard to Dr. Wilson's suggestion that it was a liver toxin, the blood serum showed no sign of increased bile content.

The CHAIRMAN said that Dr. Wilson's comments were significant in view of his work published in *Brain*,<sup>1</sup> concerning cases of degenerative changes in the lenticular nucleus in association with changes in the liver in the form of cirrhosis lasting for many years. Here there seemed to be nothing pointing to definite liver disease or to disorder of internal capsule or basal ganglia. But it seemed clear that this child's mother had some psychosis while pregnant with her, so that she inherited an instability of the nervous system. The notes did not say whether she had delirium with the febrile attacks. It was not surprising that such a child should have a mental breakdown, and he regarded

<sup>1</sup> *Brain*, 1912, xxxiv, pp. 295-509.

the case as an unsatisfactory one. Though she might recover from this attack, he felt sure she would remain nervously and mentally unstable; possibly she would become an early case of dementia.

Dr. BROWN in reply, said that there were no mental symptoms or choreic movements in the previous attacks of vomiting, &c. The only sign of rheumatic affection was that the child had had what were described as "growing pains," and a somewhat obscure cardiac condition, probably insufficiency of the mitral valve. The heart's apex was displaced outwards. The bruits had now disappeared. There was now in the hospital a girl, aged 20, who was suffering from chorea and who became acutely maniacal and confused. She was in a similar state to that in which this girl had been, only worse, and she had a high temperature. He agreed that this child was very intelligent, but had been subjected to intellectual pressure. She had a toxæmia of intestinal origin, as shown by the decomposition which went on in the alimentary tract, and by the benefit which followed the use of intestinal antiseptics.

## Section of Psychiatry.

January 28, 1913.

Sir GEORGE H. SAVAGE, President of the Section, in the Chair.

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### The Neuropathic Inheritance.

By F. W. MOTT, M.D., F.R.S.

#### SYNOPSIS.

##### (I)

- (1) Insanity and the neuropathic inheritance.
- (2) Temperament and heredity—Galton's researches.
- (3) Mendelism and the neuropathic inheritance. The researches of Dr. Weekes and Dr. Davenport.
- (4) The neuropathic inheritance in relation to genius and insanity, suicide, degeneracy, selfishness, and neuroses.

##### (II) THE INVESTIGATION OF RELATIVES IN THE LONDON COUNTY ASYLUMS.

- (1) The analysis of 3,118 cases.
- (2) Antedating or anticipation statistics and pedigrees showing this mode of elimination of unsound elements from a stock. Data relating to 508 insane offspring of 464 insane parents. Collateral heredity and antedating.
- (3) Study of neuropathic inheritance by pedigrees. A number of selected pedigrees to show points of interest.
- (4) Single compared with dual neuropathic inheritance.
- (5) Propagation of the insane in relation to hereditary transmission.

(III) A STUDY OF GENERAL PARALYSIS IN RELATION TO  
NEUROPATHIC INHERITANCE.

- (1) The incidence of general paralysis in families where there have been two members of the family in the London County Asylums.
- (2) Comparison of incidence of general paralysis amongst resident related cases and general paralytics resident in the asylums.
- (3) Comparison of death incidence from general paralysis amongst total deaths during the last five years in the London Asylums, and incidence of general paralysis amongst related cases that have died.

(IV) THE CREATION OF THE NEUROPATHIC INHERITANCE IN  
HEALTHY STOCKS.

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INSANITY AND THE NEUROPATHIC INHERITANCE.

There are individuals born of mentally and physically sound stocks that no acquired conditions—e.g., disease, drink, poisons, engendered within the body or taken in from without, head injuries, emotional shock, distress, and even profound misery and destitution combined—can render insane. There are others, and these are in most cases derived from a neuropathic stock, whose mental equilibrium may be disturbed by any one of these conditions or even without any apparent cause, except the physiological conditions appertaining to the functions of the sexual glands at puberty and during adolescence, the puerperium, lactation, and the climacteric period of women. Between these two extremes are all gradations of mentality from the congenital imbecile and the insane adolescent dement at one end of the scale to the potential sound mind and body that no combination of acquired conditions can render permanently insane. Maudsley, in his "Pathology of Mind," has truly said: "A person does not inherit insanity, but a tendency or predisposition to it; and secondly, the tendency is inherited from the stock, and not from any particular development of it in the parentage. It is easy to understand that it is not in special individual outcomes, but in the foundation of the family nature, that we must search for the foundation of insanity." Following this wise advice, every case of insanity should be regarded as a biological problem, and the study resolves itself into the acquirement of a knowledge of what an individual is born

with—Nature, and what has happened after birth—Nurture. The former can only be approximately ascertained by the study of the ancestral stocks, requiring a careful inquiry and analysis of the family histories of the members in the direct line, and if possible of the collaterals. By careful attention and inquiries many important facts in respect to the transmission of a neuropathic taint can be obtained. It must always be remembered that the neuropathic tendency may be manifested in different members of the stock in different ways.

#### TEMPERAMENT AND HEREDITY.

Just as the bodily features are transmitted from one generation to another so is the temperament. The inborn raw material of character is the complex sum total of the fixed and organized characters of the species and the sex, modified by special racial and family characters. The former are dependent upon complexes of primitive states of feeling and cognition based upon the appetites and desires and the appropriate instinctive reactions for their satisfaction thereby ensuring the preservation of the individual and the species. The instinctive reactions are associated with concomitant primitive emotional states of feeling and objective manifestations peculiar to the sex and the species. The oldest phylogenetically, they are common to all human beings and are the mainspring of all human action, and this fact has been poetically expressed by Schiller in the following lines:—

“Durch Hunger und durch Liebe,  
Erhält sich die Weltgetriebe.”

The special racial and family characters are of later development, therefore are far less fixed, stable and organized in the nervous system, consequently are more liable to mutation. A child is born into the world with inborn immutable and mutable characters derived from these genetic sources; of the importance of the inborn characters in future conduct there can be no doubt; in proof thereof I need only remind you of Galton's remarkable inquiry into the history of twins. He found that similar twins (developed from one ovum and therefore identical germ plasm) living in a different environment remained similar in temperament and character, while dissimilar twins brought up and living in the same environment remained dissimilar; these dissimilar twins, however, were the product of two separate ova with dissimilar germs.

Again, Galton although he formulated a law of ancestral inheritance which appears to be contradictory to the accepted Mendelian law,

certainly recognized that the law only applied to masses of people, and not to individual cases, for he said: "Though one half of each child may be said to be derived from either parent yet he may receive a heritage from a distant progenitor which neither of his parents possessed as personal characteristics."

Galton also made a statistical inquiry into the inheritance of good and bad tempers, and his conclusions were that one set of influences tends to mix good and bad tempers in a family at haphazard; another tends to assimilate them, or that they shall all be good or all be bad; a third set tends to divide families into contracted portions. Moreover, he showed that there is always a tendency to revert to the normal average of the race—the law of filial regression. The older and more fixed a character is, the more liable is it to this law of filial regression.

A study of the neuropathic inheritance generally accords with Galton's inquiries on tempers. Still, the subject which is of paramount importance and interest in heredity now is: Can Mendelism be applied to human characters?

#### MENDELISM AND THE NEUROPATHIC INHERITANCE.

Professor Pearson, while entirely admitting segregation of unit characters, says: No evidence exists of Mendelian proportions occurring in the transmission of obvious human unit characters—e.g., pigment and absence of pigment (albinism). Professor Bateson does not affirm that it has *been proved* for human characters although he believes that it exists, for he says: "Organisms may be regarded as composed to a great extent of separate factors by virtue of which they possess their various characters or attributes. These factors are detachable and may be recombined in various ways. It thus becomes possible to institute a factorial analysis of an individual."

How far such analysis can be carried we do not yet know, but we have the certainty that it extends far, and ample indications in supposing that we should probably be right in assuming that it covers most of the features *whether of mind or of body*, which distinguish the various members of a mixed population like that of which we form a part.

From such a representation we pass to the obvious conclusion that an individual parent is unable to pass on to offspring a factor which he or she does not possess. Since those individuals only which are possessed of the factors can pass them on to their offspring, so the offspring of those that are destitute of these elements (nulliplex) do not



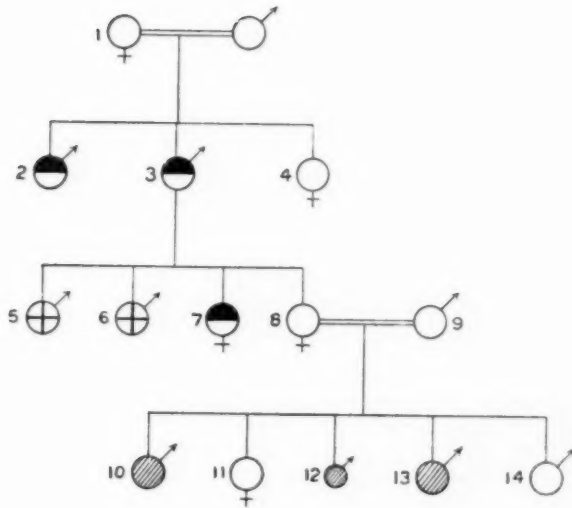


FIG. 1.

The above pedigree shows the transmission of insanity, immorality and violent temper. No. 1, the grandmother, was immoral; was found in bed with another man by her husband and son. Of her children, No. 2, an engine-driver, was "a man of violent temper who smashed things on a wholesale scale at home. He died with the delusion that he was going to heaven on the footplate of an engine." No. 3 was also a man with a violent temper, dangerous to himself and others, who eventually died from general paralysis. The daughter, No. 4, was criminally immoral; she had an illegitimate child, but no children by her marriage. The children of No. 3 are as follows: Nos. 5 and 6, both men with violent tempers, drunken and immoral; No. 7, a daughter, criminally immoral, who eventually was detained in Bethlem for a period. No. 8 is a woman with a very violent temper, smashes things, and has attacked her husband with a poker, &c.; has tried to commit suicide by poison and once by hanging; gushes to every man, but repels her husband. The husband asks, "Is she mad or bad, or both?" The husband is a healthy, robust man who comes from a good healthy stock. The children were five in number; two survive (Nos. 11 and 14), and these fortunately resemble the father; they are healthy, robust and energetic. The firstborn, No. 10, was a boy resembling his mother; he was nervous, reserved, lacked mental energy, and was prone to somnambulism and night terrors, which existed in his mother's family; he died under an operation at the age of 12. No. 12 was the image of his father, but died from measles when 10 months old. No. 13 was nervous and resembled his mother; at 19 months he died from whooping-cough.

acquire them in successive generations, but continue to perpetuate the type which exists by reason of the deficiency.

Dr. Weekes and Dr. Davenport have recently published a remarkable paper on "The Inheritance of Epilepsy," which they claim shows Mendelism in the inheritance of this disease and imbecility. It is a research of great value apart from theoretical considerations on account of the number of pedigrees recorded, but it appears to me to be open to several criticisms. Schuster, in a review, thus sums up the paper: "The inheritance of epilepsy and feeble-mindedness can be briefly stated as follows: Such very different conditions as epilepsy and feeble-mindedness must indicate some essential difference in the germ plasm, and the tables which the authors produce show a distinct tendency towards the specific inheritance of these two characters separately; thus the proportion of children who are epileptics born of parents who are both epileptic is higher than when one parent is epileptic and the other feeble-minded, and considerably higher than where both are feeble-minded." It seems to me that there is an inherent fallacy in assuming that epilepsy and feeble-mindedness can own the same cause—viz., an absence in the gametes of one and the same germinal determinant or specific factor.

"Dr. Weekes assumes the presence in the zygote of a particular factor or determiner necessary to ensure normal development. If it is absent, feeble-mindedness or epilepsy will be the result. Individuals in whom it is absent are called 'nulliplex'; according to the older terminology they would be styled pure recessives or homozygous with regard to the absence of this particular factor.

"The term 'simplex' is used to describe the heterozygote. Simplex individuals are said to possess an intermediate mental status, though some are apparently normal. It is nowhere precisely stated what are the symptoms of the 'intermediate mental states.' But the majority of persons classified in the tables as simplex are either alcoholic or neurotic. Persons who are really normal are called duplex. They have the normal development determiner twice over or are homozygous with regard to its presence." If this theory be correct, as Schuster remarks, then when nulliplex mates with nulliplex one would expect to find the offspring all nulliplex. In other words, the children of parents who are both feeble-minded or epileptic should be all feeble-minded or epileptic themselves. His own tables, however, show this not to be the case. When the Mendelian proportions are not borne out the authors endeavour to explain the fact in various ways: thus when the nulliplex

feeble-minded and epileptic offspring are in excess of expectation the excess is accounted for by parental alcoholism. Schuster points out another and more obvious explanation—viz., the manner in which the material was collected which had the effect of ensuring at least one epileptic in almost all the fraternities investigated.

Bateson has recently said: "It should be explicitly stated, however, that in the case of the ordinary attributes of man we have as yet unimpeachable evidence of the manifestation of this system of descent for one set of characters only—namely, the colour of the eyes. Moreover, if the evidence as to normal characteristics of man is defective, which in view of the extreme difficulty of applying accurate research to normal humanity is scarcely surprising, there is in respect to numerous human abnormalities abundant evidence that a factorial system of descent is followed."

This may be true for certain well-defined abnormalities, but as applied to the inheritance of the neuropathic tendency Mendelian proportions cannot be shown, according to my experience, and this is not surprising, considering the many forms in which it exists; and even if we take epilepsy, which is perhaps the most easily determinable of all conditions, yet there must be many undiscovered forms which would elude even an expert inquiry concerning the members of the stock affected.

#### THE NEUROPATHIC INHERITANCE.

"Like tends to beget like," but a collection of statistics and pedigrees merely relating to the existence in members of a stock of certified insanity or "fits," or weak-mindedness, is quite inadequate for scientific purposes, as the neuropathic predisposition manifests itself in many different forms, and it is necessary to know something of the temperament and conduct of all the members of a fraternity and as many of the stock as possible to make scientific deductions of value; and this requires time and patient investigation by a skilled person. It is very important to seek the first stages and less obvious condition of degeneration in the stock.

Morel, who studied this question more than fifty years ago, pointed out that nervous irritable weakness, the neurotic temperament, neurasthenic predisposition, may be the first evidence of degeneration of a stock. The inborn morbid temperament may be manifested in a variety of ways by the behaviour and conduct observed in various members of

the stock. The signs of degeneracy which may be exhibited are self-centred narrow-mindedness in religious beliefs, fanaticism, mysticism, spiritism, an unwholesome contempt for traditional custom, social usages, and morality, a vain spirit of spurious art and culture, a false, self-loving vanity in the pursuit of a sentimental altruism, or by eccentricities and anti-crusades and perversions of every kind, the intelligence being well preserved; such signs of degeneracy are often combined with talent and even genius, especially of the constructive imaginative order; but the brilliant intellectual qualities of a degenerate are generally associated with either a lack of moral sense or of sound judgment and highest control. Nevertheless, these neuropathics often serve a useful purpose by their disregard of tradition and social usages. Time, chance, circumstances and opportunities play an especially important part in moulding and determining the career of a neurotic stock; circumstances and environment may favour one member and he rises on the tide of fortune to an eminent position, whereas another, unfortunate or less fortunate, but with a similar inborn temperament, dies in an asylum or commits suicide in despair.

#### GENIUS AND THE NEUROPATHIC INHERITANCE.

The genius of imagination of the prophet, the poet, the artist, the patriot, and the philosopher, and lust for action of the world's great leaders of men, are so frequently associated directly or indirectly with the neuropathic taint, that Dryden's lines have become a recognized truism:—

"Great wits to madness sure is near allied,  
And thin partitions do their walls divide."

The ancients recognized the close association of genius and madness. All the greatest benefits of Greece have sprung from madness, said Pliny; there is no mind without a mixture of madness said Aristotle; he also stated that under the influence of congestion of the brain there were persons who became great poets, prophets and sybils ("Problemata," sec. xxx). How true this is may be gathered from the fact that the world's history has been made by men who were either epileptics, insane, or born of a neuropathic stock. Alexander the Great, Julius Cæsar, Napoleon, Peter the Great, Frederick the Great, Pitt Earl of Chatham, and Mahomet. The Apostle Paul, Martin Luther, Emanuel Swedenborg, and a host of names of lesser fame may be recalled. When we turn to the poets—and I will content myself by

referring to the English poets—we call to mind the names of Cowper, Wordsworth, Byron, Burns, Chatterton, Thomson, who were either insane or possessed the neuropathic temperament; in fact, that mutation of temperament from the “honourable ordinary” which tends to genius may also lead to insanity in some members of the stock, and not infrequently to the combination of genius and insanity in one individual. We do not know how it comes about that a genius springs up from an unknown source; with a meteor-like flash he appears and disappears. The imaginative faculty may be artificially stimulated by drugs and alcohol. De Quincey is said to have derived his imagination from the opium habit he had contracted; Hartley Coleridge likewise; and it is said that the “Ancient Mariner” was the result of dreams or hallucinations due to opium. But it is the temperamental inheritance which is essential for poets such as Byron, Wordsworth, and Burns; they were born and not made, nevertheless their history shows that they possessed the neuropathic temperament or inheritance.

The influence of Nature and nurture on the mind of Byron can be best divined by his own description in “Childe Harold” :—

“I have thought,  
Too long and darkly till my brain became,  
In its own eddy boiling, and o’er wrought,  
A whirling gulf of fantasy and flame,  
And thus untaught in youth to tame,  
My springs of life were poisoned.”

It is said that Byron was subject to attacks of epilepsy; the most trifling circumstances would cause him to swoon. He had seizures with convulsions. This noble poet was the child of passion, born in bitterness and nurtured in convulsions. His maternal grandmother suffered from melancholia and committed suicide; another relative took poison. His mother was eccentric. His father, who was known as “Mad Jack Byron,” committed suicide. So that there was a marked neuropathic taint on both sides in the progenitors of this greatest of poets.

Charles Lamb’s father was insane, also his sister. Dorothy Wordsworth, the sister of the poet, died insane; his daughter Catherine suffered from epilepsy, and another is said to have suffered with periodic insanity. Pope’s mother suffered from senile dementia. Dean Swift’s uncle died insane. James Thomson’s father suffered from paralysis; his mother from melancholia. Cowper inherited insanity from both maternal and paternal stocks; he was insane, and several times

attempted to commit suicide. In a letter to Lady Hesketh he says: "Could I be translated to Paradise, unless I could leave my body behind me my melancholy would cleave to me there." His descriptive account in his autobiography of his feelings is a remarkable picture of depressive insanity.

Many of these poetic geniuses suffered with the pangs of indigestion, embittered by the pangs of poverty and neglect, and their fame is posthumous. Burns, writing to a friend, said: "Canst thou not minister to a mind diseased? Canst thou speak peace and rest to a soul lost in a sea of troubles without one friendly star to guide her course, and dreading that the next surge may overwhelm her? Canst thou give to a frame, trembling alive to the tortures of suspense, the stability of a rock that braves the blast? If thou canst not do the least of these, why wouldst thou disturb me in my miseries with thy inquiries after me?"

From early life Scotland's immortal poet was subject to a disordered stomach, a disposition to headache and irregular action of the heart. He describes in one of his letters the horrors of his complaint: "I have been for some time pining under secret wretchedness. The pang of disappointment, the sting of pride and some wandering state of remorse settle on my life like vultures when my attention is not called away by the claims of society or the vagaries of the muse. Even in the hour of social mirth my gaiety is the madness of an intoxicated criminal under the hands of an executioner. My constitution was blasted *ab origine* with a deep, incurable taint of melancholy that poisoned my existence."

These revelations make one think of the truth of what Nietzsche exclaims: "Who would dare to glance at the desert of the bitterest and most superfluous agonies of spirit in which probably the most productive men of all ages have pined away?"

There can be no question but that the morbid irritability which many men of genius have manifested was but a defect of bodily derangement upon a sensitive mind. Byron, in one of his letters, said: "I am suffering from what my physician terms gastric irritation. My spirits are sadly depressed. I have taken a brisk cathartic, and tomorrow Richard will be himself again."

It is recorded that Voltaire and an Englishman, after a long conversation on the evils of this world, made a compact to die together the next day. The Englishman appeared and expected Voltaire to keep his promise, but the cynical genius thus expressed the change of his mental

attitude: "Ah! monsieur, pardonnez-moi, j'ai bien dormi, mon lavement a bien opéré, et le soleil est tout à fait clair aujourd'hui."

The fame of immortals is too often posthumous, for at all periods in history a new religion, social progress, or even scientific advancement which overthrows established customs, usages and traditions, have been too often regarded by the mass of the people either as works of the devil, of wicked men, or of madmen. Bacon, in his "Advancement of Learning," is almost prophetic of his own fate, when he says: "The doctrines in greatest vogue among the people are either the contentious and quarrelsome, or the showy and empty; that is, such as may entrap

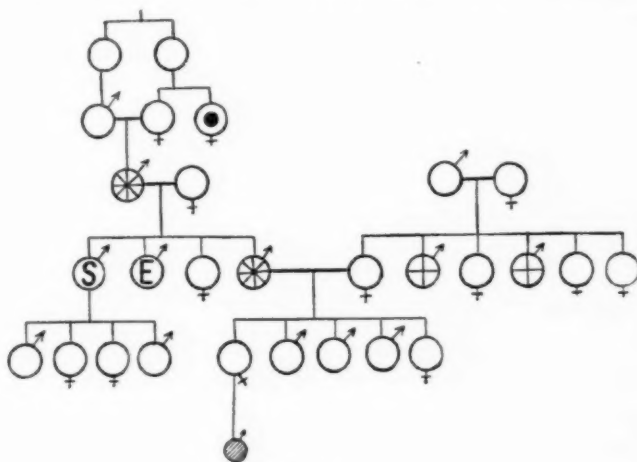


FIG. 2.

A pedigree, illustrating the marriage of first cousins. A genius was the result; he married a healthy woman, and their family consisted of an eldest son, a suicide; a second son, an epileptic; a daughter, healthy, unmarried; and a son, a genius. This man was a genius, but had an extremely well balanced mind; all his five children are healthy in spite of collateral inheritance on both sides. Circles with black centres, physically unsound. Circles in quadrants, alcoholism. Circles in octants, genius.

the assent or lull the mind to rest, whence, of course, the greatest geniuses of all ages have suffered violence, whilst out of regard of their own character they submitted to the judgment of the time and the populace. And thus, when any more sublime speculations happened to appear, they were commonly tossed and extinguished by the wrath of popular opinion."



## DEGENERACY AND SUCCESSFUL SELFISHNESS.

How often may it be observed that an apparently sound stock may in reality be unsound. Successful men in the eyes of the world may be really degenerates; not infrequently so-called self-made men form the first step in the process of degeneration. The selfishness and meanness or the cunning avarice and moral guile by which they have succeeded in selfishly amassing a fortune for their children to spend selfishly is the first evidence of degeneracy; but whereas the parents, to gratify their selfish desires, succeeded by work and abstemiousness, the children, possessing the same selfish instinct, with no need to work, and supplied with abundant wealth, acquire vicious habits and criminal propensities, and not infrequently terminate their careers in the madhouse or prison.

I have often found in the collecting of pedigrees the association of insanity and suicide in a stock preceded by, or associated with, the existence of individuals possessing the melancholic, suspicious, brooding, self-centred, hypochondriacal temperament; and it is not uncommon for suicide of one or more members of the stock in successive generations to occur. Associated with these temperamental evidences of degeneracy of a stock may be chronic alcoholism, dipsomania, hysteria, hypochondriasis, exophthalmic goitre, neurasthenia, psychasthenia, migraine, petit mal, or neuroses of an epileptic character, often unrecognized, because not manifesting fits of the major form of the disease. In searching for the neuropathic tendency there are, therefore, many possibilities of missing the inborn factor of a neurosis or psychosis though a careful inquiry be made, even when aided by intelligent co-operation on the part of the friends.

## THE INVESTIGATION OF RELATIVES IN THE LONDON COUNTY ASYLUMS.

I will now pass on to a summary of the work which has been done in the Pathological Laboratory on heredity in relation to insanity. Four years ago I initiated a card system of relatives who are at present, or have been, in the London County Asylums. The reason for doing so was to see if the anatomical features of the brain—the organ of mind—showed like the physiognomy features of resemblance in the fissures. Dr. Edgar Schuster has carefully examined and reported on the brains of a mother and daughter and of two brothers, and in a long and valuable communication has demonstrated the many points of similarity that exist. Since there is a correlation of structure and function throughout Nature we may presume that this affords an indication of a resemblance in the raw material of mentality in members of the same family.

TABLE SHOWING NUMBER OF CASES REPORTED FROM EACH ASYLUM.

| Asylum           | DIED |     | DISCHARGED |     | TRANSFERRED |    | RESIDENT |     | TOTAL |       | TOTAL<br>M.<br>and F. |
|------------------|------|-----|------------|-----|-------------|----|----------|-----|-------|-------|-----------------------|
|                  | M.   | F.  | M.         | F.  | M.          | F. | M.       | F.  | M.    | F.    |                       |
| Banstead ...     | 63   | 55  | 30         | 40  | 5           | 3  | 74       | 66  | 172   | 164   | 336                   |
| Bexley ...       | 48   | 61  | 39         | 47  | 7           | 8  | 117      | 113 | 211   | 229   | 440                   |
| Cane Hill ...    | 37   | 31  | 15         | 19  | 11          | 7  | 52       | 108 | 115   | 165   | 280                   |
| Claybury ...     | 55   | 67  | 38         | 57  | 10          | 17 | 81       | 125 | 184   | 266   | 450                   |
| Colney Hatch ... | 93   | 88  | 57         | 71  | 4           | 7  | 103      | 142 | 257   | 308   | 565                   |
| Hanwell ...      | 51   | 48  | 34         | 60  | 7           | 5  | 63       | 136 | 155   | 249   | 404                   |
| Horton ...       | 39   | 27  | 21         | 27  | 10          | 8  | 83       | 101 | 153   | 163   | 316                   |
| Long Grove ...   | 12   | 9   | 25         | 33  | 3           | 5  | 64       | 88  | 104   | 135   | 239                   |
| The Manor ...    | —    | 13  | —          | 11  | —           | 2  | 1        | 44  | 1     | 70    | 71                    |
| The Colony ...   | 2    | —   | 1          | —   | 3           | —  | 9        | 2   | 15    | 2     | 17                    |
| Total ...        | 400  | 399 | 260        | 365 | 60          | 62 | 647      | 925 | 1,367 | 1,751 | 3,118                 |

TABLE SHOWING PROPORTION OF DEATHS AND RECOVERIES AMONGST "RELATIVE" CASES.

|             | Discharged              | Transferred            | Died                    | Resident                  | Total |
|-------------|-------------------------|------------------------|-------------------------|---------------------------|-------|
| Males ...   | 260 = 19·0<br>per cent. | 60 = 4·4<br>per cent.  | 400 = 29·2<br>per cent. | 647 = 47·3<br>per cent.   | 1,367 |
| Females ... | 365 = 20·8<br>per cent. | 62 = 3·5<br>per cent.  | 399 = 22·7<br>per cent. | 925 = 52·8<br>per cent.   | 1,751 |
| Total ...   | 625 = 20·0<br>per cent. | 122 = 3·9<br>per cent. | 799 = 25·6<br>per cent. | 1,572 = 50·4<br>per cent. | 3,118 |

From a few hundred cases at the commencement of the inquiry the list has rapidly increased until it has now reached 3,118 cases. This has involved a vast amount of work, and I wish to express my indebtedness to all the superintendents and medical officers, to the Clerk of the Asylums Committee and his staff, and to my assistants, especially Mr. Mann, for the assistance they have afforded me in this inquiry. It would take far too long a time to give more than a summary of the results obtained. There is yet a good deal to be done, but I think the following conclusions may be arrived at:—

The 3,118 cases are made up from 1,450 families. At the present time in the London County Asylums there are 725 so closely related as parents and offspring, brothers and sisters. A priori, this, to my mind, is striking proof of the importance of heredity in relation to insanity, for we cannot suppose that 20,000 people of the four and a half millions of people in the County of London brought together from some random cause would show such a large number closely related as 3·6 per cent. The large number of cases from this Asylum probably represents the

**Total—3,118 cases made up from 1,450 families.**

They show the following facts:—

(1) In the insane offspring of insane parents daughters are much more numerous than sons.

(2) Amongst insane members of the same family (brothers and sisters) sisters are more numerous than brothers.

This fact may be correlated with the fact that more women are in asylums than men. About one-half of the people in the London asylums at the present time have, according to an admirably lucid report of the Clerk to the Asylums Committee, been resident more than ten years. The silting up in the London asylums at the rate of 125 to 200 per annum is largely due to women. There are several reasons for this: general paralysis, which is a fatal disease, is three times more frequent in men than in women; the recoveries in women do not bear the same proportion as in men. Now, why should women be more liable to become insane than men? I will briefly summarize the causes which, in my opinion, are operative:—

The physiological emergencies connected with reproduction—i.e., the menstrual periods, child-bearing, and the cessation of the period of reproduction, the climacterium; moreover, there is a more unstable mental equilibrium in women. I would also add as an important, and perhaps the only *cause* in many instances—the enforced suppression by modern social conditions of the reproductive functions and the maternal instincts in women of an emotional temperament and mental instability.

#### ANTICIPATION OR ANTEDATING.

Dr. Maudsley has observed that Nature tends to mend or end a degenerate stock. Now, how could Nature best mend or end a degenerate stock? By segregating in a relatively few germs all the unsound elements, leaving the others free—as it were, a crystallization out of the diseased elements. What would this do? you may ask. Well, it would make some of the offspring so weak by intensifying the disease and bringing it on at an earlier age that they would, if left to Nature's process of elimination, be killed off early, or unfitted for propagation by being brought into the asylums in adolescence. This was termed by Darwin "antedating" or "anticipation," and I have found that there is a signal tendency in the insane offspring of insane parents for the insanity to occur at an earlier age and in a more intense form in a large proportion of cases; for the form of insanity is usually either congenital imbecility or the primary dementia of adolescence, which

generally is an incurable disease. This is statistically shown in the figures regarding the age at the time of first attack in the insane offspring of insane parents. You will observe that nearly 50 per cent. of these insane offspring had their first attack of insanity at or before the age of 25, and whereas in the case of the insane parents advancing age apparently brings greater liability to insanity, in the case of offspring, with advancing age the liability to insanity tends rapidly to diminish. Now, besides the fact that this shows Nature's method of eliminating unsound elements of a stock, it has another important bearing, for it shows that after the age of 25 there is a greatly decreasing liability of the offspring of insane parents to become insane, and therefore on the question of advising marriage of the offspring of an insane parent this is of great importance. Sir George Savage recently said in his presidential address that this statistical proof of mine accorded with his own experience, and that if an individual who had such an hereditary taint had passed the age of 25, and never previously shown any signs, he would probably be free, and he would offer no objection to marriage.

Pedigrees and statistical data relating to antedating appear to show an intensification and anticipation by a coalescence or crystallization out of the unsound germinal determinants into a few of the offspring, leaving the germ plasm of the others free. This would not only purify the stock by segregation, but the diseased offspring would be unfit for the struggle for existence and propagation. In putting forward this theory of coalescence of similar diseased germinal determinants, I may mention in support of it a statement made by Galton in his great work on natural inheritance. "In the process of transmission by inheritance elements derived from the same ancestor are apt to appear in large groups, just as if they had clung together in the pre-embryonic stage, as perhaps they did."

STATISTICAL DATA RELATING TO INHERITANCE AND INSANITY,  
ESPECIALLY IN RELATION TO ANTICIPATION.

From an investigation of the age at the time of first attack in 508 pairs of parent and offspring (from the records of 464 insane parents of 500 insane offspring) the following table has been compiled. The figures denote the percentage of cases whose first attack occurred within the given age-periods.

| Age-periods    | Father | Offspring | Mother | Offspring |
|----------------|--------|-----------|--------|-----------|
| Under 20 years | 1.4    | 26.2      | 0.6    | 27.8      |
| 20-24 years    | 0.4    | 18.0      | 3.4    | 15.7      |
| 25-29 "        | 1.4    | 18.0      | 4.4    | 18.2      |
| 30-34 "        | 9.6    | 13.0      | 7.8    | 13.4      |
| 35-39 "        | 11.5   | 7.3       | 9.2    | 10.0      |
| 40-44 "        | 9.2    | 6.4       | 10.3   | 5.8       |
| 45-49 "        | 14.3   | 6.0       | 12.0   | 3.7       |
| 50-54 "        | 17.5   | 0.9       | 12.3   | 2.4       |
| 55-59 "        | 13.8   | 3.7       | 14.0   | 1.7       |
| 60-64 "        | 10.1   | —         | 11.6   | 1.3       |
| 65-69 "        | 5.0    | —         | 8.8    | —         |
| 70-74 "        | 4.6    | 0.4       | 3.1    | —         |
| 75-79 "        | 0.4    | —         | 1.3    | —         |
| 80 "           | 0.4    | —         | 0.6    | —         |

Adolescence  
Involutional  
period

These figures are shown graphically in the following diagrams (fig. 3), the abscissæ representing the age-periods and the ordinates the percent-

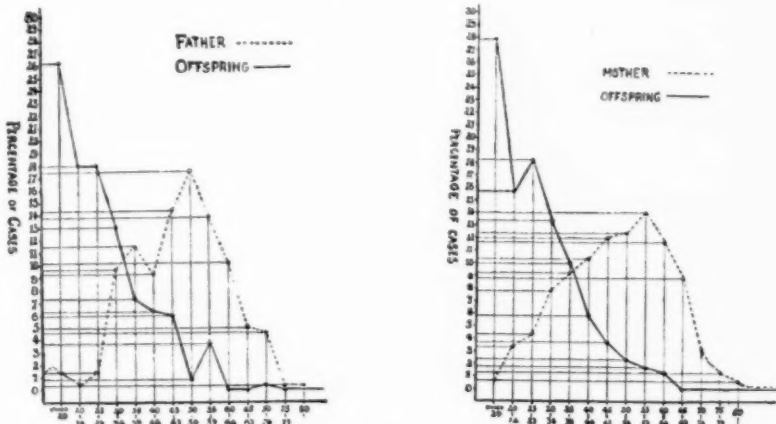


FIG. 3.

A comparison of these two curves shows a notable difference in the dotted line curves of the two parents. The curve of the mothers rises steadily and progressively from 20-55. The curve of the fathers does not commence to rise till after 25; there is a small peak at 35-39. This is the period when general paralysis is most likely to occur. But the main difference in the curves of fathers and mothers is due to the incidence of child-bearing, which causes the steady rise to the climacterium in the maternal curve.

age of cases whose age at the time of first attack falls within the given periods. They clearly show the signal tendency to the occurrence of most of the insanity in the offspring of insane parents at a much earlier age than in the parent; that is to say, antedating or anticipation is the rule.

Investigating the ages at the time of first attack in the insane offspring of insane parents, I find in the following pairs that 239, or 47·8 per cent. out of 500 offspring, had their first attack at or before the age of 25 :—

|                        |   |
|------------------------|---|
| Mother—son ... ..      | 51 out of 118 offspring                   |
| Mother—daughter ... .. | 81 „ 170 „                                |
| Father—son ... ..      | 45 „ 90 „                                 |
| Father—daughter ... .. | 62 „ 122 „                                |
| Total ... ..           | 239 out of 500 offspring = 47·8 per cent. |

The following table shows the average age at the time of first attack in the parent and offspring :—

|  | Parent | Offspring |
|--|--------|-----------|
| 120 pairs mother—daughter ... ..                                       | 49·7   | 29·3      |
| 67 „ mother—son ... ..   | 50·2   | 30·7      |
| 76 „ father—daughter ... ..  | 50·1   | 30·4      |
| 51 „ father—son ... ..   | 51·9   | 33·1      |
| 79 parents, 133 offspring in families with more than two insane ... .. | 47·7   | 28·7      |
| Total, 393 parents, 427 offspring ... ..                               | 49·7   | 30·0      |

In addition there were 71 parents whose average age was 49 at the time of first attack who were associated with imbecile offspring.

Lastly, I find that in 299, or 58·8 per cent., of the 508 pairs of insane parent and offspring the first attack in the offspring occurred at an age 20 or more years earlier than in the parent; of these 299 instances 73 of the offspring were imbeciles.

#### COLLATERAL HEREDITY.

When collateral heredity is studied the same signal tendency to occurrence of anticipation or antedating is shown, as the following tables and curves prove.

The subjoined table is compiled from 193 pairs of uncles and aunts with nieces and nephews in which only collateral heredity is manifested, and 231 pairs of uncles and aunts with nieces or nephews, in which are included those instances where one or both parents of the nieces and nephews are also insane. The figures denote the percentage of cases whose first attack occurred within the given age-periods.



| Age-periods    | Collateral only |                 | Collateral and direct |                 | Involuntary<br>period |
|----------------|-----------------|-----------------|-----------------------|-----------------|-----------------------|
|                | Uncle or aunt   | Niece or nephew | Uncle or aunt         | Niece or nephew |                       |
| Under 20 years | ...             | 5.2             | ...                   | 20.7            | ...                   |
| 20-24 years    | ...             | 3.1             | ...                   | 19.2            | ...                   |
| 25-29 "        | ...             | 6.2             | ...                   | 3.4             | ...                   |
| 30-34 "        | ...             | 12.9            | ...                   | 7.8             | ...                   |
| 35-39 "        | ...             | 11.9            | ...                   | 14.3            | ...                   |
| 40-44 "        | ...             | 11.3            | ...                   | 12.1            | ...                   |
| 45-49 "        | ...             | 12.4            | ...                   | 10.4            | ...                   |
| 50-54 "        | ...             | 14.5            | ...                   | 4.3             | ...                   |
| 55-59 "        | ...             | 7.7             | ...                   | 2.1             | ...                   |
| 60-64 "        | ...             | 8.8             | ...                   | 12.1            | ...                   |
| 65-69 "        | ...             | 1.5             | ...                   | 8.2             | ...                   |
| 70-74 "        | ...             | 1.0             | ...                   | 1.7             | ...                   |
| 75-79 "        | ...             | 3.1             | ...                   | 2.1             | ...                   |
| 80 "           | ...             | —               | ...                   | —               | ...                   |

These figures are shown graphically in the following diagrams, the abscissæ representing the age-periods and the ordinates the percentage of cases whose age at the time of first attack falls within the given periods (fig. 4).

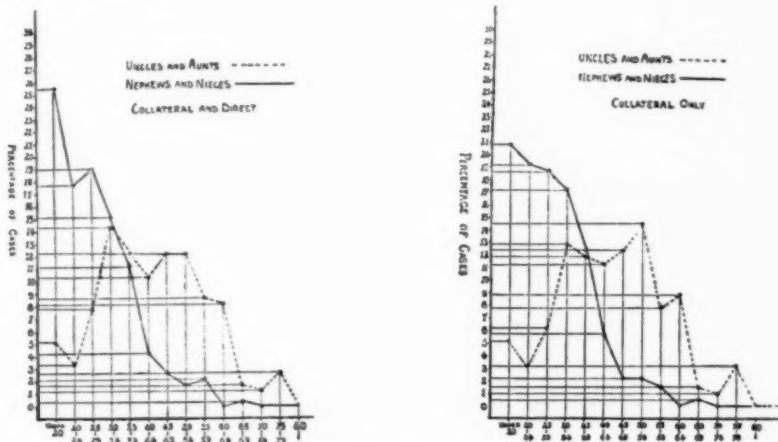


FIG. 4.

A comparison of these two curves shows that the tendency to anticipation or antedating is less marked when there is only collateral inheritance; it will be observed that the offspring curve slopes very gradually in comparison with that of parent and offspring, as well as with that of collateral and direct.

Of the insane nieces and nephews of insane uncles and aunts, 103 out of 208, or 49.5 per cent., had their first attack at or before the age of 25:—

|                       |     |     |                        |
|-----------------------|-----|-----|------------------------|
| Uncle—nephew or niece | ... | ... | 51 out of 93           |
| Aunt—nephew or niece  | ... | ... | 52 „ 115               |
| Total                 | ... | 103 | „ 208 = 49.5 per cent. |

## STUDY OF THE NEUROPATHIC INHERITANCE BY PEDIGREES.

I have already published in my Presidential Address to the Neurological Section some pedigrees illustrating the points of my argument regarding anticipation,<sup>1</sup> but I propose to show a few of these and other new ones; moreover, Dr. Hill Wilson White will, later, refer to twenty-four pedigrees which he has most carefully investigated.

## SOME FAMILY RECORDS SHOWING ANTICIPATION.

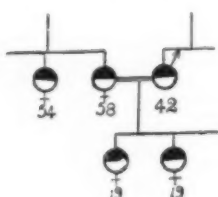


FIG. 5.

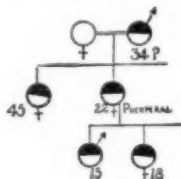


FIG. 6.

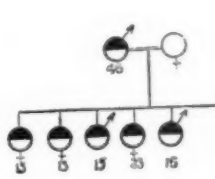


FIG. 7.

Figs. 5, 6, and 7.—Three pedigrees to illustrate "antedating"; the onset of insanity in the offspring is shown to occur at a much earlier age than in the parents. These pedigrees also illustrate extreme cases of hereditary transmission of the neuropathic taint; as a rule, not more than one insane offspring of an insane parent occurs in four or five. The occurrence of insanity in all the children is probably due to the fact that there is a double insane inheritance in all these instances, although it is only shown in one completely, and one partially.

## PEDIGREES SHOWING ANTICIPATING.

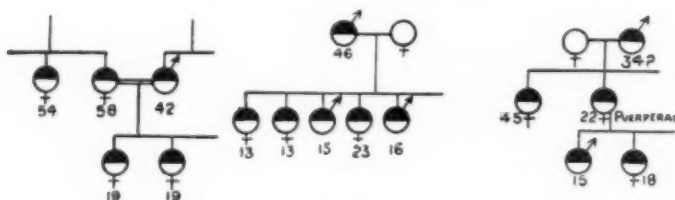


FIG. 8.

Three pedigrees to illustrate "antedating"; the onset of insanity in the offspring is shown to occur at a much earlier age than in the parents. These pedigrees also illustrate extreme cases of hereditary transmission of the neuropathic taint; as a rule, not more than one insane offspring of an insane parent occurs in four or five. The occurrence of insanity in all the children is probably due to the fact that there is a double insane inheritance in all these instances, although it is only shown in one completely, and one partially.

<sup>1</sup> *Proceedings*, 1912, v (Neur. Sect.), pp. 15-20.

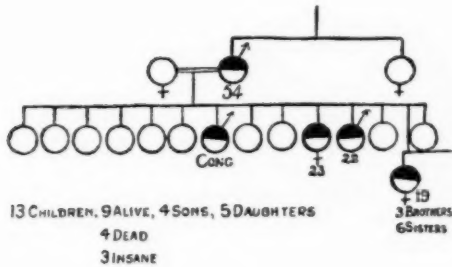


FIG. 9.

A. B., an alien Jew, aged 54, was admitted to an asylum for the first time, suffering with involutional melancholia; he has a sister who has not been in an asylum, but, as events turned out, bore the latent seeds of insanity. The man is married to a healthy woman who bore him a large family; the first six are quite healthy, then comes a congenital imbecile epileptic (cong.), then two healthy children, followed by a daughter who became insane at age of 23, then a son insane at age of 22, and lastly two children who are up to the present free from any taint. The sister of A. B. is married, and has a family of ten—seven girls and three boys; one of the females was admitted to the asylum at the age of 19, and since this pedigree was constructed a brother of hers has been admitted, aged 24. Half-black circles are insane. This pedigree is instructive: it shows direct and collateral heredity; it also shows remarkably well the signal tendency to the occurrence of insanity at an early age in the children of an insane and potentially insane parent.

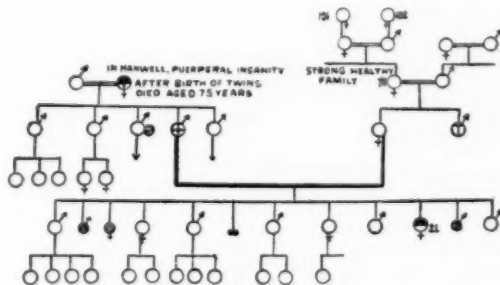


FIG. 10.

In the above pedigree is shown the mating of a female descendant of a strong healthy family with longevity to the drunken son of a drunken mother, who also had an attack of puerperal insanity. Of the children from this marriage three died young; the one affected member became insane in adolescence and has died of tuberculosis in the asylum (half-black circle), whilst the remainder are apparently healthy, and those who are married have healthy children.

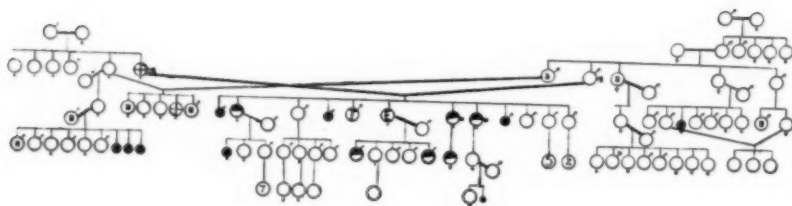


FIG. 11.

This pedigree is of interest in showing the marriage of two brothers with two sisters. In the first instance the male suffered with heart affection, which was transmitted to the offspring. In the second case the female suffered from cirrhosis of the liver and paraplegia, and was probably alcoholic and possibly syphilitic. The result was three insane and one epileptic offspring. From the first insane daughter the issue was apparently unaffected; but from the next daughter, who had masked epilepsy, of five children born two were insane. The next two insane daughters each gave birth to an illegitimate child by the same father; one of these children became insane at adolescence, whereas the other has married and has an apparently healthy child. H denotes heart affection. Half-black circles, insanity.

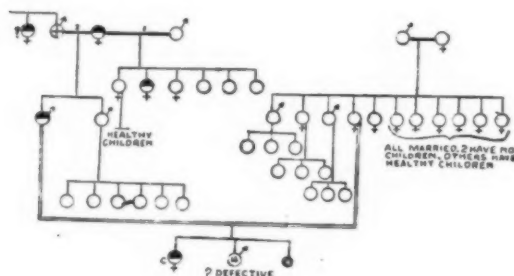


FIG. 12.

This pedigree commences with an insane woman who first marries an apparently healthy man, and of their six children one becomes insane. She next marries a drunkard whose sister is reported to be insane. The result of this marriage was a weak-minded son, who came into the asylum at the age of 42, and an apparently normal son, who marries and has healthy children. The insane son married a woman coming from a good stock, with the result that their firstborn daughter is an imbecile, and the second born, a son, is mentally defective.

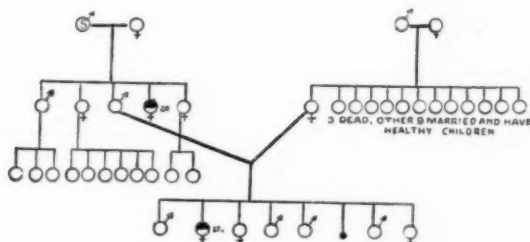


FIG. 13.

This pedigree shows the hereditary taint, commencing with suicide (s) in the grandfather and insanity in the next two generations; in each generation the affected member was cut off by adolescent insanity.

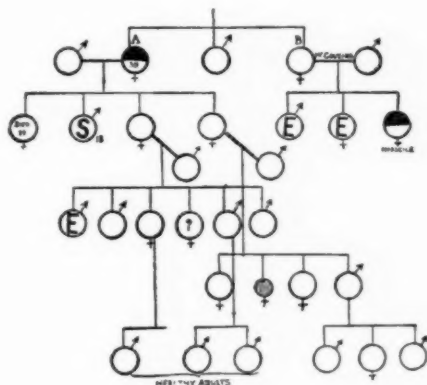


FIG. 14.

This pedigree shows the result of marriage of first cousins, in both of whom there was a latent neuropathic taint. The family consisted of three individuals—two sisters, A and B, and an elder brother, who was married but had no family. B married a first cousin, and although neither of them were insane nor epileptic, yet they had two children epileptic and one a congenital imbecile; this terminated the stock on that side. That there was latent insanity was shown by the result of the marriage and the fact that a sister became insane. A, however, married into a healthy, virile stock; she became insane at the age of 38. Although living many years after she never recovered; the exciting cause was the death of a son by suicide (S) at the age of 18. There were two daughters who became mothers of families; the eldest son of one suffered with masked epilepsy, but no other evidence of neuropathy was shown in this generation. The taint seems to have disappeared, inasmuch as there are healthy, grown-up members of the fourth generation.

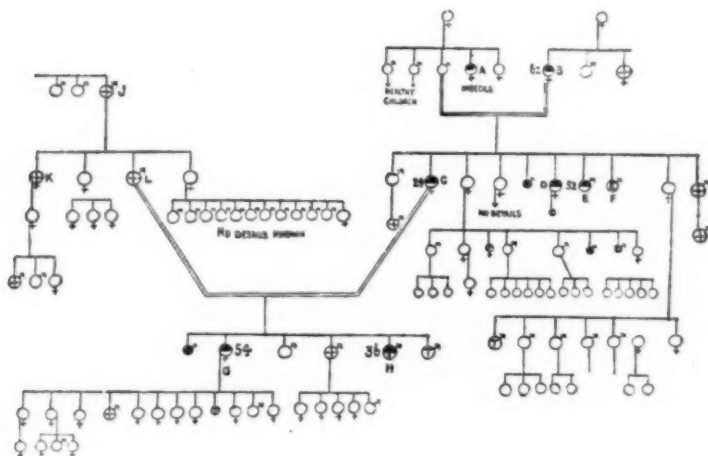


FIG. 15.

Pedigree showing the apparent elimination of the unsound elements in a stock with dual insane inheritance. A, an imbecile, but was never put away. B, became insane at the age of 62; melancholia; in Colney Hatch Asylum for nine months, but eventually died in Caterham Asylum. C, became insane at the age of 24 (St. Luke's Asylum) after the birth of her first child, which died in infancy; she was discharged after five months; her next attack occurred at the age of 38 (when suckling her last child), when she was in Hanwell for twenty months with acute mania; at the age of 43 she was admitted to Colney Hatch and died there seventeen months later. D, very peculiar and eccentric, but was never put away; she married twice, and by her first husband had one child which died in infancy from convulsions, by her second husband no children; she died between 40 and 50 years; described by her relatives as insane. E, became insane at the age of 52, acute mania, and died after three days' residence in Hanwell; had been in feeble health for years and had suffered from lead colic on two occasions. F, epileptic fits from infancy; admitted to Hanwell Asylum at the age of 28; after seventeen years' residence was transferred to Glamorgan County Asylum. G, became insane at the climacteric period; admitted to Cane Hill at the age of 54; chronic mania; teetotaler; her children and grandchildren, with the exception of one son aged 26 who "drinks and bets," are not affected. H, has had delirium tremens; married an alcoholic, now in Islington Infirmary; no children; first certified at the age of 36 and has been in and out of asylums ever since; has been in Claybury Asylum five times, and other asylums besides; in features he is supposed to resemble his paternal grandfather, but in versatility and humour apparently resembles his maternal grandfather, who was a famous clown. J, K, L, are reported to be alcoholic, but in spite of this they all lived to good ages. J died at the age of 78; K is still living, over 70 years of age; and L died at the age of 74. Longevity is a characteristic of this stock.

Professor Karl Pearson, writing to *Nature*, November 21, 1912, "On an Apparent Fallacy in the Statistical Treatment of 'Antedating' in the Inheritance of Pathological Conditions," criticizes on mathematical grounds the evidence of anticipation. I do not feel myself competent to reply to the opinion of such an eminent authority on mathematics

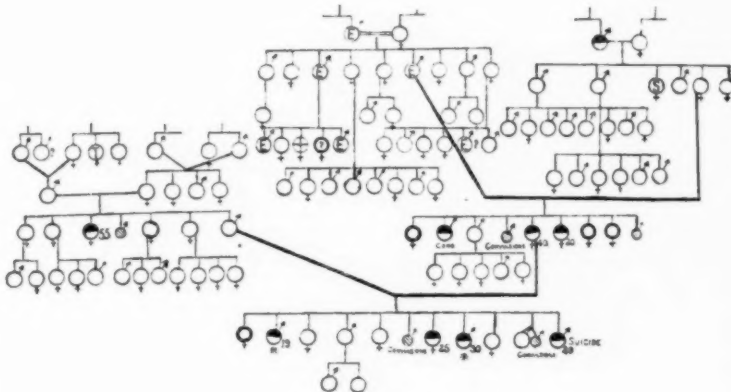


FIG. 16.

A very comprehensive and interesting pedigree obtained for me by Dr. Wilson White, showing the result of marriage of a nearly sound stock in which the temperament was, generally speaking, of the sanguine type; there was only one member insane at fifty-five, she was unmarried; her four sisters, who were all married, had some healthy, grown-up children. The brother himself, perfectly sane and healthy, married a woman descended from stocks in one of which there were many members suffering with epilepsy (E); indeed, her father and her grandfather suffered with it. On the maternal side there was suicide (S) of an aunt and insanity of a grandfather; most of the members of this stock were of a melancholy, brooding temperament. The result of the mating of these two neuropathic stocks is shown. There were nine children—of which three, marked with deep black-rimmed circles, suffered from some form of neurosis; a male congenital imbecile; a healthy male who has five healthy children; a child who died in early life of convulsions; the patient's mother who became insane at the age of 40; a female who became insane at the age of 20; two females also suffered with some form of neurosis; lastly, a male who died in early infancy. The next generation shows the result of mating this unsound stock with an almost healthy, sound stock. There are not as many unsound members as in the last generation, and we observe that the four members that became insane at the ages of 19, 25, 30, and 20, all had their first attack at a much earlier age than their mother; one of these committed suicide and two were found dead. This pedigree illustrates well the signal tendency to the occurrence of antedating. The sound members of the stock apparently inherited their temperament from the father's side, and the one member that is married has quite healthy children; this looks as if the unsound elements of this degenerate stock had been cleared out by segregation of the unsound germinal determinants, causing intensification of the disease and occurrence of the onset at an early age, thus preventing propagation.



applied to biometrics, but it does not militate against my conclusions, nor explain away the fact that a large proportion of the insane offspring of insane parents are affected with imbecility or adolescent insanity; for granting the assumption that there is no antedating at all, we might rightly expect the ages at onset of the insane offspring of insane parents to be comparable with the ages at onset of all the admissions to the asylums during the same period. This is by no means the case, for

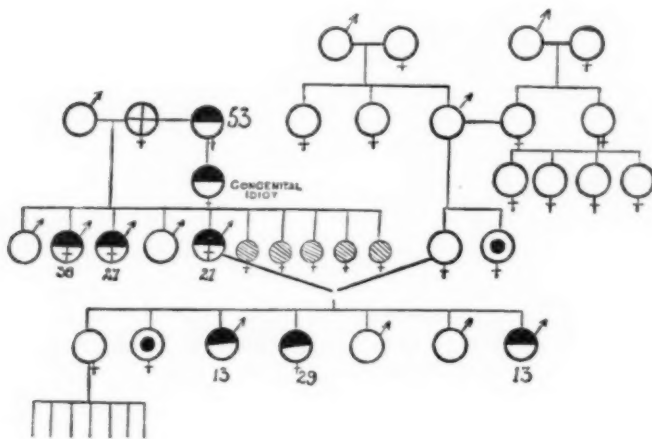


FIG. 17.

A family of drunken and insane people. The figures with half-black circles are insane; the same with the cross indicate drink and insanity; the circles with only a cross indicate excessive drinking. The two stocks show a marked difference; one side, the maternal, is practically free from any taint; almost every member of the paternal stock is unsound. The degeneracy commenced with a drunken woman whose sister died, aged 53, in Colney Hatch Asylum, where she had been twenty years; she had a congenital imbecile daughter in Leavesden. The result of mating a sound individual with a drunken woman with insane predisposition is shown in the members of the family born: a son healthy, then two alcoholic sons who were insane at the ages of 36 and 27, then a healthy son, then another alcoholic son, who also was insane at the age of 27; finally, five daughters who died in early life, probably through the neglect of a drunken mother, indicated by small, shaded, circular figures. One member of this drunken and insane family married into a healthy sound stock. Seven children were the fruit of this marriage; of these, two sons and a daughter were normal, and three were insane, two of them having become insane at the age of 13. The clear circle with a black centre indicates bodily disease. I used to give this pedigree as an instance of drink causing insanity, but after the establishment of the card system of relatives I found the notes of the sister of the drunken grandmother; she was an inmate of Colney Hatch for twenty years. It sometimes happens that the one is taken and the other left, and it would have been a benefit to society if the drunken progenitor of this degenerate stock had been taken.

amongst the insane offspring there is a far greater proportion affected in early life.

I may say that the examination of pedigrees first led me to regard antedating as Nature's method for eliminating the unfit, and the pedigrees, which are numerous, that I have since obtained all strengthen the opinion. I hope shortly to publish a large number of these pedigrees and further elaborated statistics on the question of antedating, obtained from a further collection of data since the above figures were obtained.

Professor Pearson in one way does not deny the fact that there is a tendency for an insane stock to be either ended or mended, which is really an important practical point we have to decide, for he says: "In the case of insanity is the man or woman who develops insanity at an early age as likely to become a parent as one who develops it at a later age? I think there is not a doubt as to the answer to be given; those who become insane before the age of 25, even if they recover, are far less likely to become parents than those who become insane at later ages; many, indeed, of them, considering the high death-rate of the insane, will die before they could become parents of families."

Mr. Nettleship has shown that antedating occurs in other diseases, notably diabetes, and it was he who called my attention to the probability of my being able to show antedating in insanity, because I remarked that I seldom found insanity occurring in pedigrees beyond three generations; there was a tendency to elimination of the unsound members by early death.

Erasmus Darwin, the grandfather of Charles Darwin and Francis Galton, said: "As many families become gradually extinct by consumption, epilepsy, mania, it is often hazardous to marry an heiress, as she is often the last of a diseased family." In a letter to the father of Charles Darwin, probably prompted by the fact that one of his sons committed suicide, he wrote: "I know many families who had insanity on one side, and the children, now old people, have had no sign of it. If it were otherwise there would not be a family in the kingdom without epileptic, gouty, or insane people in it." Francis Galton, his other distinguished grandson by his second wife, established the law of filial regression, or the tendency to re-establish the normal average of the race. It is remarkable how this progenitor of our two greatest biologists anticipated the epoch-making discoveries of his most illustrious grandsons.

Our President has himself found in his large practice that there is a tendency for the offspring of insane parents to become insane

at an earlier age, and in the question of marriage it is of signal importance.

I shall be glad to hear the experiences of other members of the Section on this point concerning heredity and insanity.

#### SINGLE COMPARED WITH DUAL NEUROPATHIC INHERITANCE.

Every pedigree is a study in itself, and occupies a whole book if systematically carried out as regards inheritance of characters, and the classification of the same is a matter of considerable difficulty. We have not enough systematic pedigrees yet to form precise data and conclusions upon, but I may be permitted to refer to indications from the examination of pedigrees of three generations which I have obtained myself, and combined with those obtained by Dr. Wilson White, Dr. Cribb, and Dr. Daniel. I will divide them into two groups: (1) Those with a double pathological inheritance—that is, both ancestral stocks show insanity, feeble-mindedness, drunkenness, epilepsy, suicide, or nervous disease of various kinds, direct or collateral within two generations; and (2) those with a pathological inheritance on one side only.

(1) The analysis of families with a double insane inheritance, represented by insanity, suicide, nervous disease, in both paternal and maternal antecedents, direct or collateral, within two generations:—

##### Eighteen Families Examined.

| Number of children | ... | Number died young | ... | Insane, suicide, nervous disease | ... | Apparently normal |
|--------------------|-----|-------------------|-----|----------------------------------|-----|-------------------|
| 116                |     | 16                |     | 39                               |     | 61                |

39 per cent. of the offspring reaching adult age were affected.

(2) The analysis of families in which there was an insane inheritance on one side only:—

##### Ninety Families Examined.

| Number of children | ... | Number died young | ... | Insane, suicide, nervous disease | ... | Apparently normal |
|--------------------|-----|-------------------|-----|----------------------------------|-----|-------------------|
| 384                |     | 40                |     | 33                               |     | 311               |

9.6 per cent. of the offspring reaching adult age were affected.

The conclusion which may be drawn is that a child born of a dual neuropathic inheritance stands on an average a chance of being insane four times as great as where only one stock is infected. This, however, applies to the general average, and not to individual cases.

PROPAGATION OF THE INSANE IN RELATION TO HEREDITARY  
TRANSMISSION.

As a leading article in the *British Medical Journal* of May 11, 1912, refers to this question of my investigations upon anticipation tending to the ending or mending of a degenerate stock being used as an argument against measures being taken to prevent the propagation of the unfit, I particularly desire to impress upon my audience the fact that I have always laid a great stress upon the necessity of *segregating congenital imbeciles* now that Nature by man's aid does not kill them off as formerly. Moreover, it is highly desirable to follow up those members of the family who are sane, and particularly those who are discharged as cured, in order to see whether Nature has really mended that particular degenerate stock.

One of the great arguments advanced for sterilization has been that recurrent cases of insanity breed lunatics in the intervals of readmissions to the asylums. I have no doubt this is the case, but before Parliament would even consider such a procedure justifiable it would require the strongest and soundest evidence that life segregation or sterilization would appreciably diminish the numbers of the insane. Single instances are attractive as copy for newspapers, and may serve as object-lessons to the public, but the Legislature will require comprehensive data and statistics. In the following table are some preliminary data relating to this question.

The following figures represent an analysis of the female admissions to three asylums during the year 1911:—

|           |     |                       |     |                    |
|-----------|-----|-----------------------|-----|--------------------|
| Hanwell   | ... | 164 female admissions | ... | 32 recurrent cases |
| Claybury  | ... | 259 " "               | ... | 64 " "             |
| Cane Hill | ... | 219 " "               | ... | 52 " "             |
| Total     |     | 642 " "               | ... | 148 " "            |

Further investigating these recurrent cases, the following figures are obtained:—

|  |     | Hanwell |     | Claybury |     | Cane Hill |
|--|-----|---------|-----|----------|-----|-----------|
| Single   | ... | 10      | ... | 23       | ... | 21        |
| Married, but no children born during lucid intervals. Involuntal insanities, &c. |     | 10      | ... | 25       | ... | 13        |
| Married, children born during lucid intervals                                    |     | 10      | ... | 10       | ... | 12        |
| No history obtainable  | ... | 2       | ... | 6        | ... | 6         |
| Total  | ... | 32      | ... | 64       | ... | 52        |

Of 642 female admissions, 148 were recurrent cases, of whom thirty-two (21 per cent.) had children between their respective dates of admission. Dr. Spark has forwarded me a list of thirty-three cases (18 per cent.) from a total of 185 recurrent female cases examined who had also given birth to children during their lucid intervals.

The inference that can be drawn is that about one-fifth of the recurrent cases, or approximately one-twentieth of the female admissions, have children after their first attack of insanity, and of thirty-one such cases examined, seventy-three children were born after the first attack of insanity in the parent. A number of these cases were puerperal insanity. I am unable to give the exact figures as to the fate of these children, but a good proportion of them died in infancy, and the majority of them would be too young for us to decide which might become insane.

Recurrent insanity and epilepsy, with which it is closely allied, in relation to hereditary transmission, offer one of the most important problems for scientific investigation by complete family histories and construction of pedigrees, and I can conceive no more important work on the relation of heredity to insanity than the following up systematically of the history of children born in the sane intervals of cases admitted several times to the asylums.

From the statistics of relatives a computation has been made of the proportion of offspring who were born after the first attack of insanity in the parent. The figures are as follows: 590 pairs of parent and offspring investigated from 529 insane parents with 581 insane offspring.

|                            |     |     |                                     |     |
|----------------------------|-----|-----|-------------------------------------|-----|
| Mother and daughter, pairs | ... | ... | 17 children born after first attack |     |
| Mother and son             | "   | ... | 9                                   | " " |
| Father and daughter        | "   | ... | 11                                  | " " |
| Father and son             | "   | ... | 9                                   | " " |
|                            |     |     | <hr/>                               |     |
| Total                      | ... | ... | 46                                  | " " |

Forty-six offspring out of 581 were born after the first attack of insanity in the parent—i.e., 7.9 per cent.

That is to say, in the case of 529 insane parents *the birth of only one-twelfth of their 581 insane children would have been prevented by sterilization or life segregation of the parent after the first attack of insanity.*

These figures refer to the offspring which become insane, *but there are a large number of offspring which do not become insane, and these would be cut off if life segregation or sterilization were adopted.*

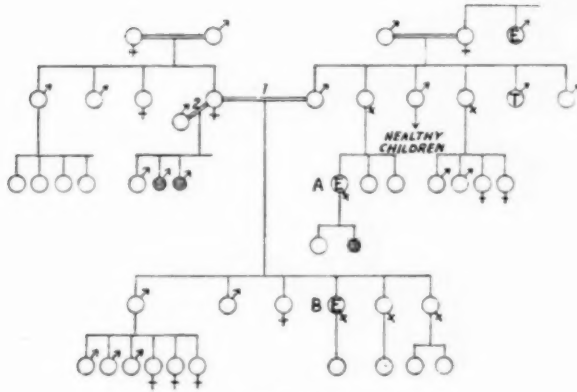


FIG. 18.

This pedigree is of interest in showing the appearance of epilepsy in two members of a stock after it had missed a generation. All other members of the stock were mentally unaffected. One of the offspring of one of the affected members (A) died from injuries received while the mother was in a fit; while the only child of the other affected member (B) was the result of seduction by her stepfather.

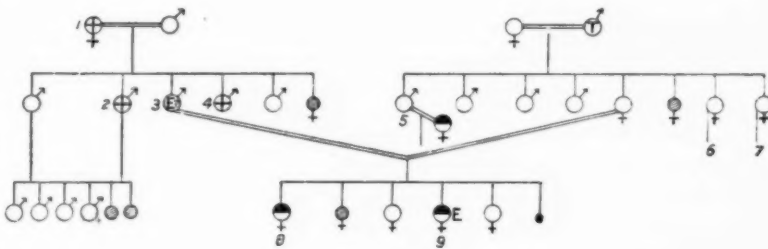


FIG. 19.

The above pedigree shows the intensification of the neuropathic taint in a stock with the elimination of the two affected members by adolescent insanity. No. 1, the grandmother, was alcoholic, and died at the age of 40. Of her children, Nos. 2, 3, and 4 were alcoholic, excitable, and violent. No. 3 "had stupors like No. 9," and eventually died from tuberculosis at the age of 36. His wife came from a comparatively good stock as shown by the fact that Nos. 5, 6, and 7 have healthy children and grandchildren, in spite of the fact that the wife of No. 5, about twenty years ago, was a resident of Banstead Asylum for a period. Of the children of No. 3: No. 8, a girl, was certified at the age of 16, and died in Claybury Asylum from tuberculosis at the age of 21. No. 9, her sister, was subject to fits, and was admitted to Claybury Asylum at the age of 21, where she is still resident. The other two sisters are exceedingly nervous and emotional.

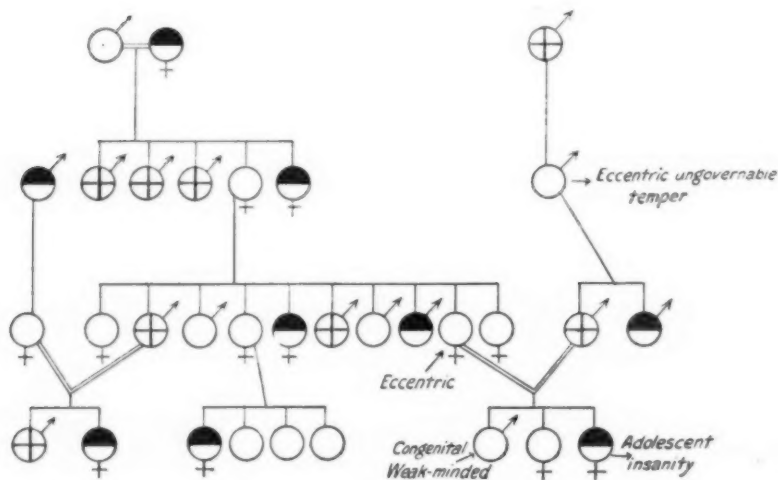


FIG. 20.

Pedigree of a well-to-do family with marked alcoholism (circles in quadrants) and insanity (half-black circles).

#### STATISTICS OF GENERAL PARALYSIS IN RELATIVES.

The incidence of general paralysis in families where *two* members have been in the London County Asylums is as follows:—

*Mother and Son.*—96 families: 8 families in which general paralysis figured—in 1 the mother was affected, in 7 the son was affected, and in none were both affected.

*Mother and Daughter.*—157 families: 3 families in which general paralysis figured—in 1 the mother was affected, in 1 the daughter was affected, and in 1 both were affected.

*Father and Son.*—78 families: 13 families in which general paralysis figured—in 5 the father was affected, in 8 the son was affected, and in none were both affected.

*Father and Daughter.*—103 families: 12 families in which general paralysis figured—in 10 the father was affected, in 1 the daughter was affected, and in 1 both were affected.

*Brothers.*—140 families: 32 families in which general paralysis figured—in 26 one brother only was affected and in 6 both were affected.



*Sisters.*—211 families : 8 families in which general paralysis figured—none in which both were affected.

*Brother and Sister.*—212 families : 18 families in which general paralysis figured—in 17 the brother was affected and in 1 the sister was affected.

*Grandparent and Offspring.*—24 families : 1 family in which the grandparent was a general paralytic.

*Collateral Pairs.*—186 families : 24 families in which general paralysis figured—in 2 families both male cousins were affected, in 2 families both uncle and nephew were affected, in 5 families one male cousin was affected, in 3 families the aunt alone was affected, in 6 families the uncle alone was affected, in 5 families the nephew alone was affected, in 1 family the niece alone was affected. As general paralysis is fatal within a year or two of admission, difficulties arise in regard to pairs of paralytics being known, unless one of the pair has been resident since the card system was initiated. Thus, to my knowledge, during the last fifteen years there have been three or four cases of husband and wife and several of father and son.

#### THE NEUROPATHIC INHERITANCE IN RELATION TO GENERAL PARALYSIS.

It is generally admitted that in the pedigrees of general paralysis of the insane, the "neuropathic taint" is not found to anything like the extent that it is in the pedigrees of patients suffering from neuroses, psychoses and feeble-mindedness. This is not surprising if we regard general paralysis as an organic disease due, like tabes, to the action of the syphilitic organism.

Our President in his Lumleian Lectures<sup>1</sup> emphasized this fact that general paralysis is not associated with an hereditary taint to anything like the extent that other forms of insanity are. I have endeavoured to investigate this question by comparative statistics of the incidence of general paralysis occurring in the 3,118 relatives who have been admitted to the London County Asylums, and the incidence in the admissions of the total population ; also by comparison of deaths from general paralysis among these two classes of individuals, and I think my results bear out the premise that the neuropathic taint does not enter as a large factor in general paralysis. I will summarize my researches on this subject as shown in the subjoined tables.

<sup>1</sup> *Lancet*, 1907, i, p. 935.

TABLE I.

*Incidence of General Paralysis amongst Residents in Asylum Population.  
1911 Report, Table E2.*

|                    |     | Males |     | Females |     | Male and female |
|--------------------|-----|-------|-----|---------|-----|-----------------|
| Total population   | ... | 8,591 | ... | 11,475  | ... | 20,066          |
| General paralytics | ... | 334   | ... | 128     | ... | 462             |
| Percentage         | ... | 3.9   | ... | 1.1     | ... | 2.3             |

*Incidence of General Paralysis amongst Resident Related Cases.*

|                     |     |     |     |     |     |       |
|---------------------|-----|-----|-----|-----|-----|-------|
| Total related cases | ... | 616 | ... | 892 | ... | 1,508 |
| General paralytics  | ... | 16  | ... | 7   | ... | 23    |
| Percentage          | ... | 2.6 | ... | 0.8 | ... | 1.5   |

The above Table I shows that whereas in the total resident population of the London County Asylums the proportion of female general paralysis patients to male general paralysis patients is 1.1 per cent. to 3.9 per cent., among the resident population of relative cases numbering 1,508 it is 0.8 per cent. females to 2.6 per cent. males; there are therefore considerably fewer males and females *pro rata* among the relatives resident.

TABLE II.

*Incidence of General Paralysis amongst Total Deaths occurring in the London County Asylums during the last Five Years.*

|                    |     | Males |     | Females |     | Males and females |
|--------------------|-----|-------|-----|---------|-----|-------------------|
| Total deaths       | ... | 4,126 | ... | 3,960   | ... | 8,106             |
| General paralytics | ... | 1,385 | ... | 349     | ... | 1,734             |
| Percentage         | ... | 33.5  | ... | 8.7     | ... | 21.3              |

*Incidence of General Paralysis amongst Related Cases that have Died.*

|                    |     |      |     |     |     |      |
|--------------------|-----|------|-----|-----|-----|------|
| Total deaths       | ... | 370  | ... | 379 | ... | 749  |
| General paralytics | ... | 142  | ... | 16  | ... | 158  |
| Percentage         | ... | 38.3 | ... | 4.2 | ... | 21.1 |

The above Table II shows that if we compare the number of deaths from general paralysis during the last five years in all the London County Asylums we find 21.3 per cent. of the total deaths were in general paralytics. Our relative cards refer to 749 deaths, and of these, as Table II shows, there were 158 cases of general paralysis, a total death-rate of 21.1 per cent. Again, comparing the deaths from general paralysis in 2,000 post-mortem examinations at Claybury, I found 23.0 per cent. of the total died from general paralysis; the slight increase no doubt was due to diagnostic error during life.

You will no doubt be struck by the relatively fewer females and the larger number of males *pro rata* among the relatives compared with

those of the total population. There is half the percentage of females, and 4 per cent. more males, although the total incidence is almost identically the same (21 per cent.). I would explain this as due to two causes :—

(1) The relatively fewer general paralytic cases occurring among the relatives is probably due to the fact that a considerable number of women admitted to the asylums suffering with general paralysis are derived from a class of female who is more likely to have suffered with syphilis than any other; they are euphemistically described as of no occupation. The prostitute either has no friends to visit her or she is disowned by her relatives, and therefore she is far less likely to appear in the relative cards.

The difference among the males is not so great and may be of no consequence, or the slight increased incidence of general paralysis among the relative cases may indicate that the neuropathic taint does play a small part in the production of general paralysis amongst these cases. The slight increase may also be due to the comparatively large number of brothers affected.

I found 18·7 per cent. of pairs of brothers affected with general paralysis of the insane. Now it may be asked, why should there be relatively such a high percentage of brothers affected, if the neuropathic tendency did not play an important part in the production of general paralysis? Its explanation is possible in three other ways.

Sir George Savage has always maintained the important influence of sexual excess, indeed, in his text-book he speaks of the general paralytic wife. I am of opinion that the ardent sexual temperament has much to do with the production of both tabes and general paralysis. A temperament is even more likely to be inherited than the "neuropathic taint." If we admit, as we must, the possibility of the existence of such a temperament in two brothers, then we can explain the frequency of the incidence by a temperamental inheritance favouring the onset of general paralysis. But it is possible that two brothers might get syphilis from the same source; there is evidence indicating that there may be a specific virus for these parasymphilitic affections. Lastly, I would suggest as a cause of this greater liability of brothers to general paralysis the possibility of an inherited immunity hypersensitivity to react to the specific organism of syphilis. In favour of this argument I advance the following premises :—

The great majority of cases of general paralysis suffer with very mild primary and secondary symptoms; tertiary signs in the form of

gummata are rarely met with, and I base this statement upon the post-mortem examination of over 500 general paralytics. The average time after infection is ten years, and it matters not whether the patient has been treated with mercury or not. Specific remedies, arsenic as well as mercury, have no curative effects. The Wassermann reaction is very pronounced in both the blood and the cerebrospinal fluid, which I regard as possibly evidence of an increased immunity hypersensibility. An excitable, neurotic man who is also erotic is more liable, if he has this immunity hypersensibility, to suffer from a premature primary decay of his nervous system ending in tabes or general paralysis.

#### THE CREATION OF THE NEUROPATHIC INHERITANCE.

If Nature is always trying to end or mend degenerate stocks, what is the reservoir from which fresh degeneracy arises? Can a sound stock be made degenerate by prolonged toxic conditions of the blood? In fact, can two germ plasms which have been long subjected to poisoned conditions of the blood undergo a pathological mutation affecting only the functions of that most complex and delicate of all organs—the brain. The poisons may be introduced into the body from without for long periods of time, as in the case of chronic alcoholism. The poison may be engendered in the body as the result of the growth of parasitic organisms—e.g., syphilis and tuberculosis; or it may be a result of disorder of the functions of one or more of the glands whose internal secretions are essential for vital activities; or glands like the liver and kidneys, which are essential for ridding the body of waste products, may fail in the performance of their functions. The blood-stream no longer under such conditions maintains its normal biochemical relation to the organs of the body; a vicious circle tends to occur in which even the specially protected structures may suffer. The brain itself may immediately or quite early feel the influence of the change in the blood, and the unpleasant symptoms aroused may thus be a protective warning to the intelligent mind, and efforts will be made to avoid the danger, if the sensibilities are not blunted by habit and tolerance. The germ cells are undoubtedly protected against the influence of poisons, but they are nourished by the same blood and lymph as the body cells; prolonged toxic conditions of the blood—e.g., by syphilis, alcoholism, and tubercle, the racial poisons—cannot but affect their specific vital energy, one manifestation of which may be irritable nervous weakness.

Admit that irritable nervous weakness—neurasthenia—may be the starting-point of an unstable nervous condition in a previously healthy stock which in successive generations may intensify under a continuance of an unfavourable environment; and admit, as we must, that this unstable nervous condition is a special outcome of modern civilization and does not exist in a primitive people living a simple mode of existence—then as fast as Nature eliminates unsound elements by ending or mending degenerate stocks, social conditions tending to neurasthenia, or nervous weakness as the term implies, may be produced by a vast number of combinations owning a social cause related to unphysiological modes of existence causing bodily and mental stress. Among the most important are prolonged poisoning of the body, including the specially protected structures, the brain and the germ cells, by indulgence in excess of alcohol, syphilis, tubercle, lead, and the drug habits; the nervous exhaustion caused by the poisons of infectious diseases, fever and bodily diseases, and the anxiety and mental pain associated therewith. The nervous exhaustion resulting from sexual excesses of all kinds, and from the mental pains arising from the ungratified natural desires of the sexual passion, from the stress of city and town life with its feverish pursuit of gain and pleasure, from competition, whether in examination, occupation or business, from the constantly increasing departure from physiological modes of life. The existence of more refined physical and mental enjoyments, bringing with them desires and emotions previously hardly known or realized; marriage without parentage and restriction of the birth of offspring, starving the maternal instinct in which is rooted the highest altruistic feelings, developing the neurotic self-regarding temperament which so frequently precedes hysteria and insanity. Then prolonged emotional stress—e.g., grief, especially the grief that “does not speak but whispers the o’er-fraught heart and bids it break”—and hatred which rankles in the breast; sudden emotional shocks—e.g., disappointment in love, loss of a dear one, and, too often among the poor, death of the bread-winner and breaking up of the home—are the exciting causes of a mental breakdown. All these depressing conditions acting on the mind produce an injurious reaction in the body, causing sleeplessness, loss of appetite, and failure of the digestive and assimilative processes. Restoration of nerve potential and the nutrition of the whole body may thus become impaired, and a vicious circle produced which by continuous expansion tends to disturb more and more the biochemical equilibrium of the body functions leading to the generation of chemical

poisons in the body or to failure of the excretory organs to eliminate poisons which should be cast out of the body. This auto-intoxication reacts upon the sensitive and exhausted brain, causing further mental depression (melancholia), or by paralysing highest control, to uncontrollable agitation and excitement (mania). It is obvious, therefore, that sociological conditions play an important part in the production of insanity; moreover, it shows that certain occupations, or no occupation, may predispose to insanity.

SUMMARY OF POINTS WHICH REQUIRE DISCUSSION AND FURTHER APPLICATION.

*Anticipation in Relation to ending or mending a Degenerate Stock.*

In my opinion I am justified in concluding that there is a signal tendency to the occurrence of insanity in the offspring of insane parents at a much earlier age. Therefore a large proportion of the parents have given birth to their insane offspring before they themselves were insane. Another point, and a very important one, which requires further investigation is this: Does the anticipation which I have shown necessarily either end or mend a degenerate stock? About the proof of the former condition there is no difficulty, for if there are no offspring, or the offspring die in early life, the stock is ended. There is, however, much more difficulty in being sure of the mending of the stock, as there are several questions still unsolved. Nature certainly attempts to mend the degenerate stock by causing the insane offspring of insane parents to suffer with congenital imbecility or primary dementia of adolescence, and thus much is done towards getting rid of unsound members; for these insane offspring would be, or should be, kept in asylums until they die; thus they would never have an opportunity of procreating. What we really want to know is, what is the fate of all the offspring and of the next generation, both of those who are sane and of those who have had an attack of insanity and are discharged as recovered? Do they breed insane or degenerate children? Have the lines of neuropathic inheritance been only partially cut off by Nature? A great many facts show that a disease may be latent and reappear in a stock when the conditions of mating or environment are favourable. Therefore, we require a collection of pedigrees which will prove conclusively that the offspring who are free from the insane manifestations during adolescence will breed children who will not become insane. This seems possible from the law of ancestral inheritance and Mendelian segre-



gation, but the proof of this must be given. Even if it can only be shown that there is a strong tendency to end or mend a degenerate stock by Nature, we shall learn by a study of these pedigrees how we can materially assist Nature in her effort—e.g., supposing it were shown that the discharged *recovered* cases bore the seeds of insanity concealed in their body by later on begetting epileptics and congenital feeble-minded (in its widest sense), or children who later become insane, a clear indication would be afforded that something should be done to prevent this propagation of the unfit.

*Secondly.*—We want to know what are the inborn characters of children born to parents who suffer with recurrent insanity. Are they more liable to become insane than the offspring of parents suffering with other forms of insanity? Again, what is the proportion of children born in the sane intervals after the first attack, and has the attack of insanity in the parent any time relation to the insanity which subsequently develops in the offspring?

*Thirdly.*—What types of insanity are especially liable to transmit an insane or neuropathic inheritance? Under what circumstances have epilepsy and anomalous forms of epilepsy a greater tendency to transmit a neuropathic taint? To ascertain this a number of pedigrees of patients require to be taken.

I am in hopes that many of the members of the Section from their knowledge and experience will criticize freely my conclusions, showing any fallacies that they think underlie them. I shall be quite as grateful for this as for support of my premises, as my object may be summed up in the words of Bacon in his "Advancement of Learning, Divine and Human":—"First, therefore, in this as in all things that are practical, we ought to cast up our account, what is in our power and what not; for the one may be dealt with by way of *alteration*, and the other by way of *application*."

#### DISCUSSION.

The PRESIDENT (Sir George Savage) said that Dr. Mott had laid before them a wealth of information. Many of the facts of this paper were confirmatory of his experience of nearly half a century. First, it was taught that all insanity was inherited; that insanity in a family affected every member of that family, so that any one of them was liable to become insane. Later, one's faith was shaken by meeting such conspicuous examples as Dr. Mott had pointed out, in which Nature re-asserted herself, and perfectly healthy families



were produced. Cases came before him in which there were three or four insane members of a family, and then suddenly a branch of that insane stock produced nothing but healthy offspring. Such facts compelled him to hark back, but now he was more convinced than ever that there was an enormously potent influence, which should be called the neuropathic influence, but the nature of which was not yet fully known. The relationship of neuropathic inheritance to other disorders had already been mentioned by the author. And one of the first to notice this was Dr. Maudsley, who regarded it as an alternation of neuroses; when a man suffering from asthma might have this replaced by an attack of insanity, and with the onset of insanity the asthma would leave him. The same was sometimes found in the case of gout and insanity, and diabetes and insanity. That was true not only of the individual but of the family, so that while the forefathers might have suffered from diabetes, the offspring were affected with insanity; or insane parentage might produce diabetic or gouty children. He had also been, for a long time, struck with the occurrence of "anticipation," though to Dr. Mott must belong the adoption of the term in this connexion. The fact that there might be healthy stock derived from insane stock, that there might be a breeding out of the disease, was so marked in his experience, that when his advice was sought as to whether "A" should be allowed to marry, though his aunt or uncle, or more still, if his father or mother were insane, he at once asked the question, "At what age did the relative break down?" His next question was, "How old is the individual?" If the person whom "A" wished to marry was not already related to his family by blood, he would not object, provided there were no previous neurosis in the persons themselves. He would be very guarded if there had been a nervous breakdown at any time, even though it was stated to have been of no importance. A point which had been brought out very strongly was this tendency to "breed out" the disease, and to revert to the normal of the race; but at present one could not say which members should or would be saved, and which would be lost. It was not just to condemn every member of an insane family to celibate life. He would say cousins must not marry if there was any neurosis in either of them; but cousins *qua* cousins might marry with impunity; indeed, it had been pointed out by Coutts, in his "Consanguineous Marriages" that the most beautiful offspring might have been the result of brothers and sisters mating. Mere consanguinity was not enough to condemn them; but if that were associated with some neurosis, then the projected marriage should be stopped, if possible. With regard to brothers suffering from general paralysis, many years ago both Sir Thomas Clouston and he had an experience of not only brothers but twins who were suffering from general paralysis. It was one of the events which made him feel that there was a neurotic tendency, though a very small one, as a factor in that disease. Some French authors had stated that with a neurotic inheritance syphilis tended to produce tabes, but that constitutional syphilis occurring in an individual without a neurotic inheritance tended to general paralysis. He did not think that could be substantiated. The question of the

possibility of an acquired character being transmissible was often brought up. He believed he had seen a certain number of instances in which members of a perfectly healthy stock, from some accident or injury—or of course from general paralysis—had developed insanity, and the offspring had been insane too. Thus it looked as if an acquired instability had been transmitted.

Dr. HILL WILSON WHITE demonstrated the book devised and used by himself at the asylums for ascertaining the pedigrees of patients, and described a number of instructive charts of families on the screen. He said he had gone through forty pedigrees in all, and twenty-five of them were very complete. The only selection he made was to choose patients with two living relatives, if possible, so as to get information on each side. The abnormality on the mother's side seemed to be greater than that on the father's side. In reference to this fact it should be noted that all the pedigrees were of female patients. With regard to the general conclusions, there were a comparatively small number of insane in the pedigrees. In most of the pedigrees which he worked out the law of anticipation was confirmed; the insanity either died out by the patient going into an asylum and not marrying, or, in many cases, the patient broke down congenitally. It had been said that from a tuberculous individual one was liable to get a tuberculous stock, but these inquiries did not bear that out. Another thing was that one could never tell, in any insane stock, where any individual would break down, nor even whether he would break down at all. All one could say was that if he did break down it would probably be at an earlier age than the parent or grandparent had broken down.

Dr. ROBERT JONES (Claybury) said he did not quite agree with the statistics. He considered that Dr. Mott did not make quite enough of the inheritance of the general paralytic. He (Dr. Jones) had as a patient the grandfather, the father, and son, suffering from general paralysis. Yet he considered that general paralysis might attack a parent and nothing be transmitted to the children. He gathered the latter was the President's view. He collected statistics in regard to 100 cases of general paralysis at Claybury—males—who had died, and about the diagnosis of which there could, therefore, be no doubt, for the post-mortem examination verified the diagnosis. That series brought out the idea which he had always entertained. In the 100 cases in which the family history was complete there was a history of paralysis—he did not say general paralysis—but often given by the patient's friends as "spinal paralysis." In two of those cases he knew the disease was general paralysis. In 28 per cent. of the 100 cases there was a history of some kind of paralysis. In addition there was a history of some member insane in a very large proportion—namely, in 38 per cent. In 18 per cent. there was a history of drink in the parents. In the ancestry, nine of the fathers and four of the mothers of the general paralysis cases were insane, twelve gave a history of epilepsy in the ancestors, and thirty-one gave a history of tuberculosis. It was against Dr. Mott's view, but he maintained strongly, from the experience he had had at Claybury, that tuberculosis often figured

in the ancestry or in the collaterals of patients who came into the Asylum. The point he wanted to lay stress upon was that general paralysis of the insane was engrafted on what had been termed the neurotic temperament or the neurasthenic temperament, yet, if he might suggest it, no definition of this had been given by Dr. Mott. What was the cause of neurasthenia? There was not always a nervous history. He appreciated the President's remarks on the alternation of asthma and insanity, and Sir Thomas Clouston's reference to influenza and insanity, when the latter considered influenza to have been responsible for lowering the nerve power of one-third of Western Europe. The ductless glands were also responsible for many cases of neurasthenia. Not long ago he had the case of a young woman who had been to many nerve specialists and had been treated as a neurasthenic case; she had "rest" treatment several times, but eventually drifted to the asylum. She seemed to him very like a case of ordinary myxœdema, but there was a distinct thyroid palpable. Dr. Mott kindly saw the case also, and they agreed that it was a neurasthenic case with symptoms of myxœdema. She died, and a very careful examination after death revealed a complete disintegration of the glandular structure of the thyroid which was shown to have been inactive. There were, probably, many cases in which the ductless glands were at fault—the suprarenal capsules, the pituitary body, the thyroid, the lymphatics, and possibly other glands of which little was yet known. Considering that syphilis was so common and that not more than 4 per cent. developed general paralysis, it must be grafted on to some neurasthenic base before it was revealed as general paralysis. He maintained strongly, and was supported by the statistics he had quoted, that general paralysis of the insane was, from the hereditary standpoint, related to the other varieties of insanity and could be transmitted to descendants, and it would be most interesting and instructive to know, from the pathological standpoint, what was the underlying physical factor of the inheritance of insanity. Another point was the following: There were so many cases of insanity at the ages of 42, 46, sometimes 56 and 63, that it showed the impossibility of ending insanity by segregation or by castration or by sterilization. Certainly in many of the cases the children were born before the occurrence of the insanity.

Dr. CRICHTON MILLER pointed out that Mendel's law was only intended to apply to unit factors in the first place. Insanity was, as Dr. Hyslop pointed out, a clinical entity. We were bound to be disappointed if we expected this law to hold in tracing the heredity of cases of insanity. Again, with regard to Galton's law, what Galton really pointed out was the *potential* contribution of each ancestor, rather than the actual contribution.

## Section of Psychiatry.

March 11, 1913.<sup>1</sup>

Sir GEORGE H. SAVAGE, President of the Section, in the Chair.

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### Two Cases for Diagnosis.

By ROBERT JONES, M.D.

*Case I.*—E. A. G., aged 35, single, no occupation. Formerly under Dr. Jones at the Earlswood Asylum with same physical symptoms as at present. Later in Leavesden Asylum. Threatened to commit suicide there, and occasionally showed signs of violence towards others, for which he was received into Claybury Asylum, May, 1911. Mental symptoms: Congenital imbecility with depression. Physical symptoms: Articulation jerky, gait ataxic; movements exhibit coarse tremor during voluntary effort; muscular grip only impaired by ataxia and tremor. Is unable to pick up fine objects (pin from table) without fixing shoulder or elbow to control movement. No paresis, no wasting; electrical reactions normal; no nystagmus, pupillary reactions sluggish; knee-jerks increased, flexor reflex response. Disks normal. Family history: Father insane and brother insane (latter died in Claybury). Mother and sister died of consumption.

*Case II.*—W. K., aged 44, married; occupation, blacksmith or farrier. Symptoms coming on for two and a half years. Formerly in Leavesden Asylum. Developed symptoms of melancholia there with suicidal tendency; attempted to strangle himself, for which he was received into Claybury, June, 1912. Mental symptoms: Irritability, depression, thinks he has "general paralysis" and thinks he is going to die. Impulsive and suicidally disposed because of his miserable bodily condition; memory for remote events good, but general progressive mental

<sup>1</sup> Meeting held at the London County Asylum, Claybury.

weakness. Physical symptoms: Ataxia, marked slurring or "sluggishness" of speech, which is getting worse; general inability to exercise physical effort with general atony of voluntary muscles; marked Rombergism; fine tremor of tongue and facial muscles; pupils react sluggishly to light, no nystagmus, disk no changes; knee-jerks increased but (?) unequally on the two sides; flexor response. Wassermann and lymphocytosis—negative. Family history: Mother and maternal aunt insane.

#### DISCUSSION.

Dr. ROBERT JONES said that cases presenting some kind of tremor were often found to be associated with mental symptoms in the asylums of London. If the mental symptoms were mild, such cases would, in the first instance, be taken into the Metropolitan Asylums Hospital at Tooting Bee, and if there found suitable and amenable to mild discipline they could be sent to either Darenth, Leavesden, or Caterham. But if they showed any signs of violence towards others or a disposition to suicide, or were cases needing more supervision than could there be obtained, they were certified as persons of unsound mind and sent to one of the London lunatic asylums. A syndrome had been described as the "Westphal-Strümpell" syndrome when such patients presented tremors such as these suffered from and which were associated with mild mental symptoms. He had been interested in the question of tremors for a long time; there were the tremors of general paralysis, of disseminated sclerosis, of hysteria, and the consequence of various toxins, of chorea, or of para-myoclonus, and he (Dr. Jones) would be glad of some elucidation in regard to the physical causation of these symptoms. The tremors here witnessed were an intentional tremor, but there had never been any exaltation beyond what was now observed during effort. There was no tremor apart from volitional action, neither had there been any nystagmus observed. The memory and the mental capacity of the elder patient were failing, but in the other case there had been no change. He was simply congenitally weak-minded and his mind, such as it was, appeared to suffer no deterioration.

Dr. S. A. K. WILSON considered the first patient an example of congenital cerebellar defect, though he could not tell without testing him objectively. The symptoms began quite early and they were of the kind that seemed not to change. Hence it was improbable that there was a progressive lesion. The general articulation and the movements seemed to point to defect on the afferent side from the cerebellum to cerebrum. There might be a congenital lesion in the superior cerebellar peduncle and in the red nucleus, and that could exist without causing nystagmus. There was no apparent sign of pyramidal defect. The younger patient was said to have a double flexor response. He found it impossible to dogmatize on the older case without

careful examination, but it did not seem to fall into line with the other, though there was some similarity of articulation. Though the Wassermann test was negative, he wondered whether the sluggishness of the pupils might not be regarded as of some significance. The Westphal-Strümpell syndrome was associated with "pseudo-sclerosis," and in that condition there was tremor; but of course it was neither a clinical nor a pathological entity. The term "pseudo-sclerosis" was applied to cases clinically resembling disseminated sclerosis, but which did not resemble them pathologically. The term was a misnomer and, like all terms beginning with "pseudo," should be given up.

Sir DAVID FERRIER, F.R.S., said his view agreed with that expressed by Dr. Wilson, that these were cerebellar cases, and that in essential points the two were alike. He did not think there was any affection of the pyramidal tracts.

Dr. JONES, in reply, said that there had been no change in the ordinary or common sensibility; both men were very ataxic and sometimes fell. There was no history of cerebral injury during early life in the congenital case and nothing to account for the onset of the tremor in the other.

### Case of "Washing Mania."

By C. T. EWART, M.D.

E. S., A FEMALE, married, admitted April 23, 1897, aged 32 (now 48) suffering from melancholia with suicidal tendencies. Believed that she gave out a strange, disagreeable odour from her body, and that this was spoken of by her neighbours. That she harboured numerous insects. Auditory hallucinations present. Of good physique. When admitted her youngest child was aged 5 months. She had a good deal of anxiety through monetary troubles. As a housewife she was cheerful, temperate, clean, and industrious. No evidence of insane heredity could be obtained. She has ever since admission been suffering from excessive menstruation, and this is becoming more profuse. In consequence her linen becomes soiled, and this appears not only to have created a delusion that she is unclean but also to have given rise to an obsession that she must constantly wash her whole body during the day.

It would be out of place on the present occasion to endeavour to attempt an elaborate explanation of this abnormal mental condition, but I would venture to advance two theories to account for the actions of the patient:—

(1) We have inherited from our prehistoric ancestors the three

cardinal instincts—self-preservation, nutrition, and sex—therefore it is possible to believe that some persons may also have inherited from them a supra-normal sense of smell capable of discerning an odour not recognizable by the ordinary individual. It is a well-known fact that the power of hearing the scream of a bat is possessed only by one man in twenty. If this supra-normality can exist in the case of one sense, why should it not be present in another? The future will probably teach us far more as to the relation between chemical composition and psychological results, and just as it is possible to construct hypnotics which have a predictable action upon that portion of the nervous system concerned with sleep, so it may be possible to invent particular odours with such particular actions on the olfactory apparatus, that in the case of hallucinations or illusions of smell there will be some hope of using an odour to cure the mental defect caused by another odour. It must be remembered that touch and smell are historically and evolutionally connected, in that contact is a necessity for their action. They are not like the eye and ear, affected by ether waves.

(2) Have we ever analysed the feminine motives in wearing exquisite clothing? Two women may love to wear beautiful clothes, and both may be put down as vain, yet in one case the motive impulse may be vanity—a mere desire for self-display—in the other the impulse is due to the true æsthetic sense, a love of the beautiful and the delicate. The first woman can be readily distinguished from the second by the fact that she is a slattern when no one is there, and that the unseen part of her apparel is of an entirely different order from that seen. The second woman becomes more and more particular about her clothing the more intimate its relation to her body. In both cases you find an emotional accompaniment of elation. If E. S. belongs to the æsthetic type, the soiling of her linen or the ever-present disagreeable odour would tend to produce feelings of pain, disgust, abhorrence, depression, unworthiness, and lead to instinctive actions which would tend to substitute the thrills of delight which accompany pleasure for the feeling-attitude of repulsion which is linked with that of pain. The one brings joy to the utmost recesses of our faculties, the other creates a feeling of dread, disgust and shame, which weakens and depresses. By "pleasure" I mean not the transitory gusts of a mere temporary enjoyment, but those sensations which bring deep peace and perfect contentment to the mind.

We ourselves look upon ourselves from different standpoints, according as to whether we wear evening dress, pyjamas, or golfing attire. The Salvation Army officer is capable of better work in his regimentals,



the hospital nurse acts up to her uniform, even a "bus" conductor becomes more civil when he is in his robes of office.

Emotions and instincts are as much the fundamentals of the mind as the skeleton, the lungs, the circulation, are the fundamentals of our body organization. They are the springs of our being and the pulse of the machine. E. S. apprehends cleanliness as the beautiful, therefore to her æsthetic sense it gives pleasure, and she strives for it. The "washing mania" is but a motor response to a sensory experience, just as the rhythm of the music of a waltz compels certain definite muscular movements. As to what is beautiful, this depends on "herd instinct," which means that you form your opinions according to the class or community to which you happen to belong.

#### DISCUSSION.

The PRESIDENT (Sir George Savage) observed that nearly all cases of washing mania had hallucinations of smell, especially if there was associated reproductive organ trouble.

Dr. ROBERT JONES said he was interested in what Dr. C. T. Ewart had said about Freud's views. There was no repression of a complex to be discovered in this case. He agreed that there was much to be said for the pleasure-pain theory of action, and in this case Dr. Ewart's view meant that the patient's conduct followed the motive derived from an æsthetic sentiment rather than the repression of a complex which had previously occupied the field of consciousness.

Dr. DEVINE said one often found that this washing mania was the symbol for a desire to purge a wrong action, and meant an attempt to restore moral purity. A similar idea was expressed in traditional writings. As an illustration one called to mind the Biblical significance attaching to leprosy, which was frequently used as a symbol of sin and moral uncleanness.

Dr. ELGEE said he had recently had a case of "washing mania." Six months after marriage the patient had a child, in consequence of which she had the idea that all the neighbours despised her. Later she thought she heard them reproaching her, and started to wash herself very often. On the case being explained to her she was induced to give up the habit.

**Case of Katatonic Stupor.**

By C. T. EWART, M.D.

E. M., A FEMALE, single; admitted April 20, 1912, aged 22, suffering from katatonic stupor. There was some rigidity, but when the resistance was overcome her limbs would remain for some considerable time in the position they were placed. There was a mild negativism, but no stereotypy, echopraxia, or echolalia. Takes her food when placed in her mouth, and is of clean habits. Will not reply to questions, but appears to grasp their meaning. Takes no interest in her surroundings and stands like a dummy wherever she is placed. She has been working well for some time, and very occasionally speaks in monosyllables. There is a slight amount of rigidity present. Has never menstruated since admission and is taking a Turkish bath weekly. No indoxyl present in urine; extremities not cyanosed. At the age of 13 the patient passed into the seventh standard, and is described as having been quick, steady, cheerful, careful, and a good worker at home. Her mother drank spirits to excess during the time of her pregnancy and died a year after the birth of the patient from the effects of drink. Her father is a soldier. No history of insanity on either side.

E. M., was a patient at Horton Asylum at the age of 14. I have obtained from the relatives the information that before entering Horton Asylum she had menstruated, but this had ceased. She menstruated regularly after her discharge until two months before admission into Claybury, and, as I have informed you, there has been a suppression here.

I had the honour, in 1911, of reading a paper before the Royal Society of Medicine, entitled "Amenorrhœal Insanity."<sup>1</sup> In it I endeavoured to prove that each person is built up of inherited "resistances" and "non-resistances." The view I take is that the germ-plasm might be thought to represent a gun, loaded in the case of "predisposition," but unloaded in the case of "immunity." The particular toxin to which the individual was susceptible would take the place of the finger pulling the trigger. In the so-called "alcoholic insanities" it does not require a large amount of alcohol to produce

<sup>1</sup> *Proceedings*, 1912, v (Obst. Sect.), pp. 81-98.

those changes in the nervous system which would necessitate incarceration in an asylum. I also attempted to show that a similar result occurred in amenorrhœa. One woman would resist this form of auto-intoxication, and as her insanity would not be due to the cessation of the flow, its re-establishment would have no direct effect on the mental state. Some other women, not being resistant, would readily succumb mentally to the toxin, and this, being the cause of the insanity, the recurrence of menstruation would establish recovery. I look upon E. M. as an amenorrhœic case, and shall be greatly disappointed should she not recover in three months after menstruation has been regularly established.

Had the case of alcoholic insanity refrained from alcohol he would never have been insane. Had the case of amenorrhœic insanity continued to menstruate regularly, she would never have broken down mentally. Why do the very few cases of alcoholic insanity which have the power of self-control to refrain from drink after discharge not relapse, and why do the others who do not so refrain make up a large proportion of the "ins" and "outs" of an asylum population? These spend on drink the money which should go to provide food, and thus the physical efficiency of the whole family is deteriorated. The children grow up and have to work for their living; lacking vital force, they become easily fatigued, mentally and bodily. To overcome this they fly to alcohol as a stimulant, and thus the ripples of alcoholic degeneracy spread in ever-widening circles.

#### DISCUSSION.

Dr. DEVINE said he did not consider this patient was a katatoniac, but that it was a case of manic-depressive insanity. She had had an attack before, and it was not of the præcox type. He believed she would get well.

Dr. LORD said the patient was at Horton Asylum during her previous attack. He never saw the patient when there, it was prior to his time; but he had studied her clinical record. To his mind this was a clear case of manic-depressive insanity in the retarded phase with the usual adolescent symptoms in addition. He thought amenorrhœal insanity had received its quietus, but apparently not, for Dr. Ewart returned gallantly to the fray. The patient came there suffering from the acute excitement of puberty, and the reason given for her going there was the onset of her first menstruation. He understood that the friends now alleged differently, but he thought the first history was probably the correct one.

Dr. EWART replied that he still considered the case was due to a toxæmic excitement associated with amenorrhœa.

**Case of Osteitis Deformans.**

By F. PAINE, M.D.

W. R., A MALE, aged 75. During the last twelve years a general enlargement of the head and thickening with deformity of ribs and some of the long bones have been noticed. During the last two and a half years, aural hallucinations, delusions of persecution, and a gradually progressive dementia, have supervened.

Chemical analysis of the urine: The amount of phosphoric anhydride passed during the twenty-four hours was decreased—viz., 1.92 gm.—and there was also a marked decrease in the amount of calcium salts passed—viz., 0.0576 gm. Specific gravity, usually about 1020, and the reaction was neutral or slightly alkaline; urea 2 per cent. No protein; no sugar. Microscopically, nothing abnormal was found.

Dr. F. PARKES WEBER thought that the bony disease in this case was a very good and extreme example of Paget's progressive osteitis deformans. It would be interesting to know if the patient's blood serum gave a negative Wassermann's reaction for syphilis, because it had been suggested on the Continent that all cases of Paget's osteitis deformans were of syphilitic origin. He (Dr. Weber) did not think so, but occasionally progressive deforming symmetrical hypertrophic osteitis was met with in children as a late manifestation of inherited syphilis, and might so closely resemble Paget's osteitis deformans in the lower extremities as to justify the term "syphilitic osteitis deformans."<sup>1</sup>

**Case of Organic Disease of the Nervous System, presenting some Features of General Paralysis of the Insane.**

By F. PAINE, M.D.

A. G., A MALE, aged 46. Ten years ago he had a "paralytic stroke" which incapacitated him from work. Three years later mental symptoms appeared—persecutory delusions with aural hallucinations. He was admitted into the asylum with some physical signs of general paralysis of the insane. Pupils inactive to light, slurring speech;

<sup>1</sup> See F. P. Weber, "A Note on Congenital Syphilitic Osteitis Deformans," *Brit. Journ. Child. Dis.*, Lond., 1908, v, p. 83.

there is spastic paraplegia and well marked aortic regurgitation is present. The patient's condition has remained stationary since admission. The cerebrospinal fluid gives a negative Wassermann reaction and no lymphocytes are present.

### Case of Cerebral Tumour, illustrating the value of the Operation of Decompression.

By F. PAINE, M.D.

E. J. R., MALE, aged 54. Five years ago an endothelioma was removed from the left frontal lobe, since when there has been progressive mental deterioration with hallucinations of smell. Motor aphasia is present, and Jacksonian fits, strictly limited to the right side of the body, occasionally occur.

### DEMONSTRATIONS.

By F. W. MOTT, M.D., F.R.S.

#### (1) *Some Recent Investigations on the Bio-chemistry of the Neurone.*

(a) THE living nerve-cell seen with the ultra-microscope. A viscous homogeneous colloidal spongio-plasm containing an enormous number of minute oval or round granules, which appear highly refractile on the dark ground; the nucleus with nucleoli is seen in the centre of the cell dark and less refractile. When the isotonic medium (cerebrospinal fluid) is replaced by water an endosmosis takes place, and the refractile granules escape; these remain discrete and exhibit a Brownian movement, but do not coalesce. It is probable that each granule consists of a colloidal fluid substance surrounded by a delicate membrane of (? lipoidal) substance. No Nissl granules or fibrils are seen.

(b) The living nerve-cell removed from an animal immediately after death is placed in a hanging drop of cerebrospinal fluid (the normal isotonic medium) containing a minute trace of vital methylene blue (Ehrlich). The hanging drop on the cover-glass is inserted into a well on a glass slip and kept at the temperature of the body. Examined

with a low power the whole cell appears of a pale delicate blue tint, including the nucleus. With an oil immersion  $\times 12$  and 4 ocular the cytoplasm is seen to owe its pale blue colour to the blue staining of the enclosing membrane of the colloidal granules. Seeing that this blue stain may indicate the presence of nascent oxygen it appears possible that this is a provision of the nerve-cell to obtain an enormous surface of oxygen encompassed in a small space, much as occurs in spongy platinum. It is possible to conceive that these granules afford some explanation regarding the chemistry of the neuron. No Nissl granules are seen, nor fibrils, but when the cell dies the former appear, and the nucleus stains deeply.

The results described must be regarded as of a preliminary nature, for on account of difficulties of technique and failure with many methods that have been tried, successful results of staining have only quite recently been obtained, although the work has been in progress more than six months, and a large number of animals have been used. The animals were in most cases guinea-pigs, used for the Wassermann reaction.

- (2) *Demonstration of Spirochæta pallida (Noguchi) in Culture Living, also Silver Dark-ground Preparation compared with Spirochæta microdentium and Spirochæta refringens.*
- (3) *Demonstration of the Changes in the Central Nervous System in a Case of Myxœdema, Cachexia Strumipriva, and Insanity, in which the Thyroid was of Normal Size but contained hardly any Glandular Substance ; the Organ consisted of Dense Fibrous Tissue and Lymphoid Tissue.*<sup>1</sup>
- (4) *Demonstration of the Changes in the Central Nervous System in Two Cases of Pellagra, one being Dr. Boe's English Case, the other Case an Egyptian from the Asylum, Cairo.*

<sup>1</sup> Dr. Mott's paper on the subject (written in conjunction with Dr. R. Brun) will be published in a future number.

## Section of Psychiatry.

March 11, 1913.

Sir GEORGE H. SAVAGE, President of the Section, in the Chair.

### Microscopical Investigation of the Nervous System in Three Cases of Spontaneous Myxœdema.<sup>1</sup>

By R. BRUN,<sup>2</sup> M.D., and F. W. MOTT, M.D., F.R.S.

IN spite of the increased interest now taken in the pathology of the thyroid gland, the literature on the microscopical condition of the nervous system in the various forms of hypothyroidism (cretinism, cachexia thyropriva (Kocher), and spontaneous myxœdema) is extremely limited. Although certain alterations, of a general character, in the nerve-centres of thyroidectomized animals have been recorded,<sup>3</sup> no systematic investigation has been published on changes occurring in the human subject dying of myxœdema. In a report on the "Cerebral Lesions in Psychoses of Toxic Origin," presented to the Fifteenth International Congress of Medicine, at Lisbon, 1906,<sup>4</sup> one of us (F. W. M.) described the chromatolytic changes of the cortical cells in one of the three now recorded cases of myxœdema; he also observed the marked change in the cells of the medulla oblongata, and for this reason he was induced to seize the opportunity when the occasion arrived of obtaining further material for microscopic examination, as one case did not seem to be sufficient for a definite statement

<sup>1</sup> From the Pathological Laboratory, London County Asylums, Claybury.

<sup>2</sup> Assistent am Hirnanatom. Institut u. an den Nervenpoliklinik der Universität in Zürich (Professor C. v. Monakow).

<sup>3</sup> W. Edmunds, "The Changes in the Central Nervous System resulting from Thyro-parathyroidectomy," *Proc. Roy. Soc. Med.*, 1912, v (Neur. Sect.), pp. 179-195.

<sup>4</sup> *Congrès internat. de Med.* (XV, Lisbonne), 1907, Sect. VII, fasc. 1, pp. 111, ff.



to be made. We are unable to find any further reference to this subject in the neurological literature of the last twelve years. We hope, therefore, that the following record of three cases, all of which died of certain grave symptoms, due, in all probability, to anatomical changes in the autonomous bulbo-motor system, will be of some interest. Unfortunately one of the three cases could only be very incompletely investigated, but owing to the fact that by its clinical aspect it completes in some respects the other two, we felt justified in including it.

#### CASE I.

##### (1) *Clinical Notes.*

S. C., aged 52, married, was admitted to Charing Cross Hospital on April 17, 1902, under Dr. F. W. Mott.

Previous history: The parents of the patient died of unknown diseases. There were sixteen children in the family; of these only one brother and two sisters (including patient) were still alive. Patient herself has had eight children, three of whom are still alive; three died early, between  $1\frac{1}{2}$  and 2 years of age, one died two days after birth and the last one was stillborn. Shortly afterwards, at the age of 45, the patient ceased to menstruate; previously she had always been regular. At the time of the menopause and since, the patient had been under treatment for anæmia; she also complained at the time of some pains in the joints, especially the elbows. Four years before admission she used to attend the out-patient department at the Charing Cross Hospital, under the care of Dr. Mott, for typical symptoms of myxœdema. Thyroid "tabloids" were prescribed and she improved greatly under treatment; she attended regularly for about fifteen months, but after that time (during the last three years) she has not been to the hospital, nor has she taken "tabloids" regularly; but only occasionally until the stock which was given to her had been used up. Just before Christmas, 1900, she seems to have had a sort of fit, falling unconscious off a chair. There was no recurrence of the fits, but she has often felt giddy since, and she says that when walking she has a sensation as if she would fall backwards, so that she did not dare to go out without another person accompanying her. She also felt very weak. Her condition becoming serious she again came to see Dr. Mott at the Hospital, on account of œdema and pain in the ankles, both having persisted now

more or less for nearly a year, the œdema, however, coming on in the evenings only. She also complained of breathlessness, giddiness, and drowsiness during the day, and of sleeping very badly; and for these symptoms she was admitted.

Present state: Patient is a cachectic and very anæmic-looking woman of pale yellowish, almost waxy complexion. The skin is dry and thickened, especially over the arms and hands, the latter being increased in size. There is also dryness of the hair, which does not fall out, however. The face is not much swollen, but shows some puffiness under the eyes. The condition of teeth fairly good. There is some œdema of the ankles. The first sound of the heart is very weak, otherwise nothing noteworthy. The pulse is 80 and weak; the morning temperature is 97° F. Hæmoglobin, 55 per cent.; urine clear, pale, acid; specific gravity 1015. No albumin. The speech is slow and monotonous. The intellect seems to be generally dull and enfeebled, and there is a slowness of thought as well as of expression, but sometimes her mind seems bright.

She was placed upon thyroid tablets, but without any improvement occurring.

April 30: The patient has been very unwell to-day; complained of pains in the abdomen and has been sick. The evening temperature is 100·4° F., pulse 108.

May 1: She is very drowsy and apathetic and speaks very little; she also vomited or spat out every nutriment as soon as she had taken it. (Paralysis of swallowing?) The pulse has risen to 136, the heart beating very feebly. No clinical signs discovered in the lungs. Respirations 24; temperature 98·2° F. There appears to be tenderness over the chest, but no objective signs of abdominal disease, and only with difficulty can she be induced to indicate pain in her abdomen.

On May 2 and 3 the condition was about the same, there was still marked tachycardia (112 to 144 in the evening), and impossibility of swallowing; the respiration rate was between 24 and 28. She did not recognize her relations who visited her. Nutrient enemata were administered but not retained.

May 4: In the morning the patient seemed somewhat better, which may be attributed to the successful employment of a drip enema in the night. She was able to take some nutriment by mouth and spoke to her husband. The pulse, however, remained still very frequent, 128 to 136. In the evening she suddenly collapsed and died.

(2) *Autopsy (May 5, 1902).*

Body poorly nourished. No œdema. Brain: Convolutions normal. In the choroid plexus of the lateral ventricles are several small whitish thickenings. Pituitary body very small. Unfortunately this was not preserved for examination. Thyroid: On removal of the larynx and trachea there is an obvious atrophy of both the lateral lobes and isthmus. In what remains of the right lateral lobe is a small yellowish nodule,  $\frac{1}{4}$  in. in size, the greater part of the atrophied gland appears to be fibrous in character, the caseous nodule has the appearance of a tubercle or gumma. Lungs very small, atrophied; no evidence of pneumonia, pleurisy, or tubercle. Heart very small; nothing noteworthy except a slight atheroma of the anterior mitral cusp. Kidneys, 3 oz. each; atrophied; capsule not adherent, though the surface is slightly granular, and there are one or two small cysts. Spleen, 4 oz.; liver, 2 lb. 2 oz., nothing noteworthy; gall-bladder normal. Uterus very thin-walled; the muscle appears degenerated, showing whitish specks and striæ. Ovaries very atrophied (size of a small bean). Apparently there was excessive involution of the reproductive organs. The larynx and trachea with the atrophied thyroid was preserved as a museum preparation. Portions of the brain and medulla were taken by Dr. Mott for examination. These were embedded in paraffin after hardening in 5 per cent. formol and subsequently in alcohol.

(3) *Microscopical Examination.*

(a) *Thyroid.*—A small piece of the atrophied right lateral lobe was cut out of the museum preparation, embedded in paraffin and sections prepared; these were stained with hæmatoxylin and eosin, and with Van Gieson's method (fig. 1). On examining these we were astonished to find the glandular tissue comparatively well preserved, the acini only being of somewhat irregular form and size, but containing plenty of apparently normal colloidal substance. The fibrous tissue, however, is markedly increased and many of the acini are atrophied. There is a marked increase of lymphoid tissue.

(b) *Nervous System.*—The various pieces of the brain and medulla oblongata embedded in paraffin after a few days' fixation have been cut with the Cambridge rocking microtome. The sections were stained with polychrome methylene blue and by Nissl's method. The pieces of cortex

were from the frontal and occipital lobes, and the chromatolysis observed had already been described by one of us (F. W. Mott) in toxic psychoses.

*Detailed Account of Microscopical Changes, especially of the  
Medulla Oblongata.*

*Nervous System.*—(1) Frontal cortex: A large number of the small and middle-sized pyramidal cells exhibit a slight degree of com-

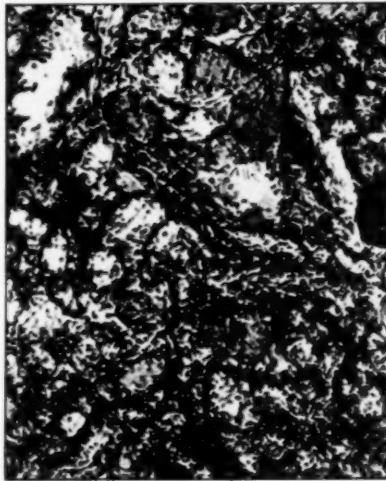


FIG. 1.

Photomicrograph of a section of the thyroid gland from Case I.  
(Magnification 140.)

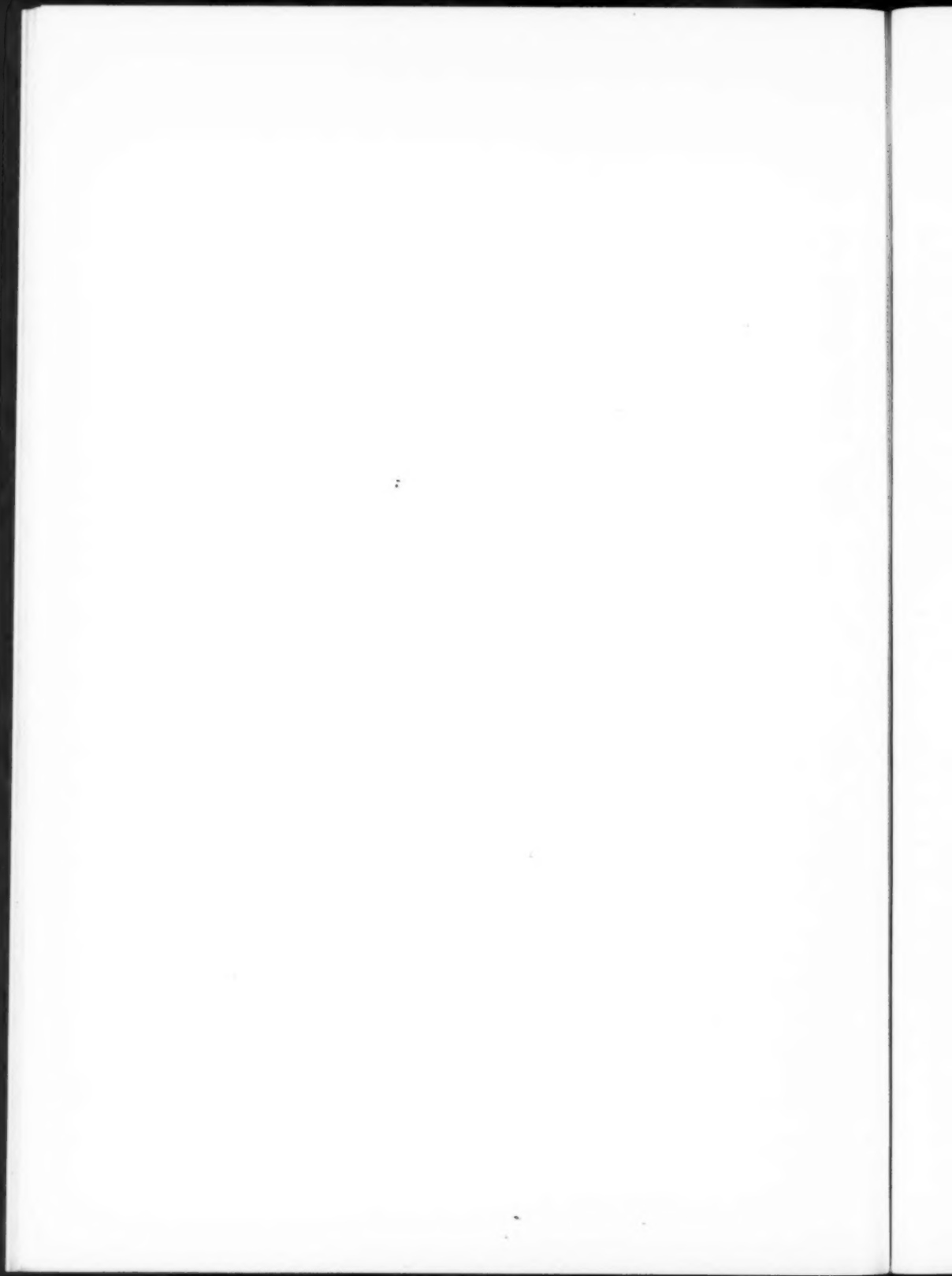
mencing chromatolysis; many of the cells show a more advanced histological change, for the nuclei are eccentric and the Nissl granules are disintegrated into a fine dust or small mass with crumbling edges, but there is little evidence of swelling of the cells. (2) Occipital cortex (calcarine): In the intergranular layer of Vicq D'Azyr a great number of the polygonal, star-like cells show marked chromatolysis; most of them exhibit nuclear eccentricity. (3) Medulla oblongata: Most of the bulbar nuclei are more or less affected, but it can be easily seen that the degree of change shown by different nuclei is very variable in intensity.

EXPLANATION OF PLATE.

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- (1) Cell groups from the nucleus ambiguus vagi, showing terminal chromatolysis: (a) Case I, (b) Case III.
- (2) Group of cells from the nucleus gelatinosus of the solitary tract (descending ninth root). Case III, advanced chromatolysis.
- (3) Group of cells from the nucleus hypoglossi, Case III, showing first degrees of chromatolysis.
- (4) Chromatolytic cells of a sympathetic ganglion of the lumbar plexus, Case III.
- (5) Nucleus dorsalis vagi, Case I. All cells show advanced chromatolysis.
- (6) Anterior horn cells of the dorsal cord, Case III. Advanced chromatolysis.







Whilst the big motor cells of the spinal accessory and hypoglossal nuclei show only a certain degree of poverty of chromatin substance, but no advanced chromatolytic changes, the groups of cells belonging to the vagus system are, without exception, in a most obvious and advanced stage of chromatolysis. In the dorsal vagus nuclei (Plate—5), most of the cells are markedly changed, a number of them showing nuclear eccentricity and a very advanced disappearance of basophile staining substance of the whole cell except at its periphery. There are also seen many shrunken, deeply stained forms without any distinct structure (vide Plate—5) being distinguishable. In the nucleus ambiguus vagi (caudal half) nearly all the cells exhibit total chromatolysis with nuclear eccentricity (Plate—1, *a*). The other association nuclei of the formatio reticularis are in various degrees but less affected. Next to the vagus nuclei the gravest changes are seen in the nuclei of the posterior columns, a number of the principal cells of both Goll's and Burdach's nuclei showing a certain amount of chromatolysis and peripheric nuclei; a few also appear slightly swollen. The big, marginal cells belonging to the nucleus gelatinosus of the descending fifth root are all more or less affected. Among the cells of the olives a considerable number are seen exhibiting chromatolysis, all cells showing an increase of yellow pigment.

#### (4) *Résumé and Conclusions.*

The history of the last five children being either stillborn or feeble suggests the possibility of a syphilitic infection. Shortly after the cessation of menstruation this woman developed gradually the syndrome of myxœdema. For fifteen months she took regularly thyroid tablets and the symptoms greatly improved. She then neglected the treatment, and did not reappear at the hospital until a severe cachexia had supervened with all the typical symptoms of myxœdema. Shortly after admission into the hospital there was a sudden aggravation of her morbid condition with obvious symptoms of acute bulbar vagal paralysis—viz., persistent tachycardia, difficulty of swallowing and of speech, accompanied by psychic disorientation (she did not recognize her relations). On the fourth day after the attack she succumbed.

Although in the case-book the impossibility of taking food by mouth is not especially denoted as a paralysis of deglutition, we have every reason to believe it really was one. First of all, the description of the condition in the clinical notes saying that the patient seemed to vomit

or "to spit out every bit of food as soon as she had taken it," then this condition being so closely associated with a persistent tachycardia and, finally, the complete absence of any anatomical change in the gastrointestinal tract found post mortem to account for these symptoms. The transitory recovery of swallowing shortly before death is not to be wondered at if we remember that quite a similar tendency towards an early re-establishment of those vital functions has often been observed similarly in many cases of acute bulbar paralysis due to thrombotic softening in the medulla. For the same reasons, we are also partly inclined to associate difficulty of speech with a suspected vagal paralysis; for even the most advanced cachexia or the most serious weakness does not, as a rule, prevent speech. This functional failure of the vagus system, although arising almost suddenly, was not altogether without prodromal symptoms, for it was noted that the heart sounds were weak and the pulse feeble on admission.

The cell changes found in the cortex and the medulla are such as correspond to a general sub-chronic intoxication: Chromatolysis of very various degrees, even in the same nucleus, without much swelling and not always followed by nuclear eccentricity. It will be noticed, however, that in the medulla the different nuclei are affected in varying degrees of intensity. The twelfth nucleus, for example, showing very little change, whereas both the dorsal and the ventral vagus nucleus are throughout affected in a most serious manner. This, again, corresponds very well with the terminal clinical stage of a fatal vagal paralysis such as was presented by our patient during the last four days of life.

As for the cortical changes, we will not go so far as to correlate these with any special functional disturbance or symptom manifested during life, except it be the slowness of speech and ideation characteristic of the disease; nor can we do more than suggest that the chromatolysis of the stellate cells of the visual cortex may be correlated with the dis-orientation and non-recognition of her friends during the last four days of her life.

Among the changes of the other bodily organs, the excessive atrophy of both ovaries deserves a more than passing consideration, for it is a well-known fact that myxœdema is especially liable to occur in women after the cessation of the sexual functions. Four cases have been reported by Saltier<sup>1</sup>: In two of these the symptoms followed a curetting,

<sup>1</sup> Saltier, "Four Cases of Myxœdema," *Australas. Med. Gaz.*, Sydney, 1911, xxx, p. 441.

and in one an oöphorectomy. Again, the statistics of hypothyroidea collected by A. R. Elliott<sup>1</sup> show that most of the cases occur in women, the proportion being seven females to one male; moreover, the majority of female cases commence at the climacteric period.

## CASE II.

(1) *Clinical Notes.*

C. O., aged 56, was admitted to Charing Cross Hospital on April 29, 1906, for a strangulated umbilical hernia. The patient had suffered from myxædema for about three years, for which, presumably, she had been treated. Two years before admission she acquired an umbilical hernia which became incarcerated on April 27, 1906, at 10 a.m.; she had then severe pains in the abdomen and during the day vomited, food first, bile later. Since then pain was continuous, but she did not vomit again. There was absolute constipation.

Present state: The patient is a stout woman of a general puffy and pallid appearance. Pulse 82, regular, of good tension; temperature sub-normal, 96·8° F.; urine acid, containing no albumin. There is a swelling in the umbilical region with a very tense, red, inflamed centre, obviously due to a strangulated hernia.

April 29, 1906: The operation was at once carried out by Mr. F. Wallis under chloroform-ether anæsthesia and offered nothing of peculiar interest. During the following night the patient slept well and had only a very slight vomiting of a little mucus; the temperature was normal, the pulse good.

May 6: Dressed. The wound has healed by first intention.

May 9: The patient is getting *non compos mentis*; she is very restless. Pulse slow, 60; respirations 16 to 18.

May 11: Mental condition much worse; she is noisy and restless, singing aloud songs and psalms.

May 12: Pulse still very slow, 54 to 62; temperature 96·4° F. Thyroid extract administered.

May 16: The mental condition remained the same. Pulse very much weaker, but still slow (64). The patient sank gradually and died.

<sup>1</sup> A. R. Elliott, "Incomplete Myxedema," *Journ. Amer. Med. Assoc.*, Chicago, 1908, L, p. 1763.

(2) *Autopsy (Twenty-six Hours after Death).*

A somewhat stout woman, body well nourished. Abdominal scar, 3 in. in length, healed by first intention. Rigor mortis present. Skull of normal thickness. Dura not adherent, normal. No escape of subdural fluid. Pia arachnoid a little congested but showing neither opalescence nor thickening. Brain: Weight 2 lb. 8 oz.; each hemisphere 1 lb. 2 oz.; cerebellum and brain stem together 5 oz. Convolutional pattern complex. Brain substance very œdematous. Ventricles not dilated. Convolutions neither flattened nor atrophic; ependyma not granular. On the under surface of the right lateral cerebellar lobe there is an irregular-shaped fossa, about as large as half a small walnut, with a thin pia arachnoid membrane; it has the appearance of an old atrophic process, the cause of which is not discoverable. Larynx and trachea normal; bronchial glands enlarged and pigmented. Thyroid: Lateral lobes small, isthmus atrophied; consistence appears normal, and upon section there is no obvious naked-eye change. Lungs slightly congested, the left showing slight œdema of the base. Heart, 9 oz.; endocardium slightly opaque; cardiac muscle soft; slight atheroma around the aorta. Omentum, some small intestines and transverse colon slightly adherent to the abdominal surface of the wound; no pus. Liver, 2 lb. 10 oz.; apparently normal; the gall-bladder contains four gall-stones. Spleen, 5 oz.; soft, normal. Kidneys, 4 oz. each, both normal. Transverse colon: A large mass of omentum is adherent; inflammatory changes present. Intestine: Nothing abnormal. Uterus: Nothing abnormal. Neither of us saw the patient during life. The brain was obtained by one of us (F. W. M).

(3) *Microscopical Examination.*

Material: (1) Some preparations from the thyroid gland stained with hæmatoxylin-eosin and with polychrome methylene blue. (2) Paraffin blocks of small pieces of the liver, spleen, heart, and kidney. (3) One paraffin block of the spinal cord (four different levels); some preparations of the ascending frontal and parietal convolutions.

The brain, unfortunately, having been thrown away, the condition of the medulla oblongata was not examined in this case.

(a) *Organs.*—The thyroid (fig. 2): Sections of the gland stained with hæmatoxylin and eosin exhibit a considerable amount of colloid sub-

stance, but the epithelial cells of the acini are very small and atrophied, most of them showing nothing more than the nucleus. Again, numbers of atrophic acini without a lumen can be seen, those consisting simply of a crowd of atrophied cells huddled together. There is also throughout the sections of the gland a very considerable increase of connective tissue and here and there small accumulations of lymphocytes are to be seen. Kidney (Van Gieson's stain): In some places the epithelial cells of the convoluted tubules appear to be swollen up and as if about to undergo desquamation, many lumina being filled with crumbling masses

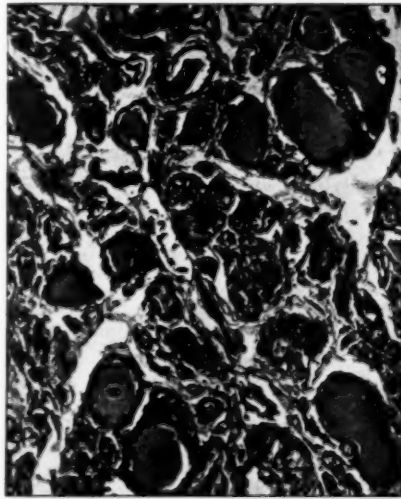


FIG. 2.

Photomicrograph of section of the thyroid gland, Case II. (Magnification 140.)

of coagulated exudation. Some arteries show their walls considerably thickened, this thickening being confined to the media and adventitia. The liver shows some increase of connective tissue surrounding the gall-ducts and veins, and some round cell infiltration of the adventitia of many arteries. The parenchyma itself seems to be intact. In the spleen nearly all the arteries show an intense endarteritis obliterans, numbers of the lumina being filled up. Heart: There is also marked endarteritis of most of the arteries of the heart; the muscle-fibres contain a great amount of brown pigment.

(b) *Nervous System*.—Anterior central convolutions: The Betz cells of the motor area do not reveal, on an average, any coarse change; yet they are not so rich in chromatin as usual, and some are even in the first stage of chromatolysis. Very few of them exhibit any evidence of advanced chromatolysis. In the sections through the posterior central convolutions no obvious changes can be seen. Spinal cord: The motor cells of the anterior horns are generally quite intact, showing well the Nissl granules, but occasionally here and there one isolated cell can be seen with commencing or even advanced chromatolysis.

#### (4) *Résumé and Conclusions from Case II.*

A woman, aged 56, and suffering for three years from myxœdema (which in all probability came on about the climacteric) has an umbilical hernia which becomes strangulated and leads to an operation. The wound heals up, and all is apparently going well until the tenth day after the operation, when an acute psychosis breaks out, with symptoms pointing to an acute mania, and accompanied by a marked slowness of the pulse which contrasts strangely with the patient's intense motor excitement. This condition persists a few days and in that short space of time leads to a fatal issue.

We have but little doubt that in this case the symptom of slowing of the heart, in spite of the motor restlessness and excitement, strongly indicates a functional disturbance of the vagus centres in the medulla, that is to say, with a state of continuous excitement of the cardiotonic vagus nucleus, a condition which probably later on led to a sudden failure or paralysis by exhaustion, causing death. We do not know whether there is a distinct connexion between this medullary condition and the psychosis or not; it may be that the latter was started by the disease of the bulbar centres or vice versa. In any case it is unfortunate that the medulla oblongata was not preserved, for it is probable that we should have found changes in the vagus nuclei, possibly of a similar character to those in the first case, but not so marked.

The arterial disease found in several of the internal organs seems suspicious of syphilitic infection.<sup>1</sup>

<sup>1</sup> This coincidence of disease with myxœdema has been noticed by two French authors, Rousay and Chatelin.

## CASE III.

(1) *Clinical Notes.*

M. McC., aged 37; occupation formerly a servant. Admission to Claybury Asylum on October 16, 1912.

No family history could be obtained, nor much of her previous life, beyond the fact that she had been in bad health for some years, and had been frequently treated for anæmia and "nerves," undergoing, among other courses of treatment, the Weir-Mitchell cure. Ten days before admission she started with a sudden attack of melancholia without obvious cause, and accompanied by vivid visual hallucinations. She spoke incoherently, weeping aloud and clasping her hands, even doing this among people in the streets; this led to the attention of the police, by whom she was taken to the infirmary and subsequently transferred to the asylum.

State on admission: A rather stoutly built woman of somewhat pasty and pale complexion. She seems very anæmic and in bad general condition of health. She was seen by one of us (F. W. Mott) a few days after admission, and the following observations were made: (Edema of the eyelids, skin and hair very dry, suggesting myxœdema. She replied to questions in a slow and wearied manner with a Scotch accent, but at the time she was seen in the laboratory she exhibited no marked mental disturbance, and it was decided that she was a case of myxœdema. A report to that effect was made to Dr. Jones, who was kind enough to send the case for diagnosis. It appeared to be the opinion of Dr. Jones that the patient was suffering with myxœdema.

The following are the notes from the case-book: Tongue foul, no teeth on the upper jaw, the other teeth are carious. Heart and lungs normal; the pulse, however, is rather slow. Urine acid, 1030 specific gravity, containing much urates and some albumin (one-sixteenth of Esbach's tube), but no casts. Nervous system: Pupils equal, reacting to both light and accommodation. There is marked slowness of speech. Knee-jerks exaggerated. Mental condition: The patient is very restless, refusing to stay in bed and to keep any clothes on. She does not know where she is nor how she got here, and talks incoherently about "God's good man," and the "lights of heaven," and says that to-morrow the world would come to an end and that nobody could help her. She gives a very rambling account of her previous life, saying that her memory



is bad. She seems to be very depressed. Therapy: 5 gr. of thyroid extract three times a day.

October 23: The patient is still very depressed, thinks that she has no friends, that she is beyond ever getting well, that she is a confirmed invalid, and a burden to her family. She shows some inclination to be ecstatic, hears the voice of God, and strips herself to pray. At night she is very restless and has to be closely watched.

October 25: Examination of the blood. It contains about 4 million erythrocytes and 12,000 leucocytes, most of them polymorphonuclears. Therefore there is no evidence of a grave anæmia, but marked leucocytosis.

October 26: The patient is becoming much weaker and is unable to swallow properly. The temperature is subnormal, 95° F., and the pulse extremely slow, never rising above 48.

October 27: There is complete inability to swallow. Nutrient enemata are not retained, but she is able to retain normal saline enemata.

October 28: The patient has remained in a semi-soporose condition, and has vomited some dark-coloured vomit. She died in the night.

(2) *Autopsy (Eleven Hours after Death).*

A stout woman with physique slightly above average and good muscular development. Teeth carious. Pupils equal, 3 mm. Dura mater *nil*. The subdural and also the subarachnoid space contain some excess of clear fluid. Pia arachnoid very little thickened, stripping readily. Sinus and vessels *nil*. Weight of the brain, 1,230 gm., each hemisphere 530 gm. (510 gm. after stripping), brain stem and cerebellum together weigh 150 gm. Brain of average convolutional pattern, showing no deformity. Some slight frontal and prefrontal wasting; no softening. The pituitary body is somewhat enlarged, causing the gland to bulge slightly over the border of the posterior clinoid processes. The bone is not eroded. The enlargement seems to be confined to the glandular portion. The thyroid is, perhaps, rather smaller in size than usual; it is pale in colour, and on section appears to be densely fibrous in parts, and shows no colloid. A small parathyroid is attached to it. Right lung free, left lung adherent along its posterior surface. Bronchi catarrhal and filled with grumous, blood-stained, viscid fluid. Both lungs broncho-pneumonic and exhibited a

commencing gangrenous patch. No visible tubercles. Pericardium free. Heart, 260 gm., atheroma, muscular substance of normal appearance. Liver, 1,570 gm., showing no marked alteration. Spleen *nil*. Both kidneys slightly granular, cortex somewhat mottled and slightly hæmorrhagic in appearance. Adrenals disintegrated. Pancreas extraordinarily long from head to tail. The head is swollen and on section shows areas of hæmorrhages in its substance. There are several small whitish areas about the size of a pin's head scattered throughout the fat in the immediate neighbourhood of the gland. Pancreatitis hæmorrhagica acuta (?) Small intestine: Several areas of petechial hæmorrhages beneath the mucous membrane. The uterus shows one small pedunculated fibroma. Left ovary cystic.

(3) *Microscopical Examination: Material and Methods.*

The brain (except the right hemisphere), the spinal cord with the spinal ganglia, a sympathetic ganglion from the lumbar plexus, the hypophysis, different parts of the thyroid, the parathyroid, pancreas and pieces of the heart, liver, spleen, and kidneys, were removed and preserved in a weak formalin solution. The right cerebral hemisphere was kept for chemical determination of the amount of calcium salts. Small pieces from the left frontal cortex, from Broca's area, and from the anterior central convolution (tongue, facial, and leg area), and from the cerebellum, from the medulla oblongata, and the spinal cord at different levels, several spinal ganglia (cervical and dorsal) and the sympathetic ganglion were cut in sections by the paraffin and celloidin methods, and stained with Nissl, Bielschowski, Weigert, and Marchi methods. Sections of the other organs were stained with hæmatoxylin-eosin and Van Gieson's methods; some sections from the pancreas were also examined by Gram's method.

(a) *Organs.*—Thyroid gland (fig. 3): The most striking change to be seen is an extreme atrophy of the glandular substance, and the colloid material was almost absent. The gland consists almost exclusively of dense fibroid tissue, and of foci of round cells scattered here and there like small islands. These crowds of round cells, as a rule, surround and include the small remaining portions of glandular epithelium. There are also in the centre of the islands of small round cells, large round epithelial cells, which are partly isolated, partly huddled together in little groups, but, as a rule, exhibiting no lumen, corresponding to the centre of acini. Very rarely, but here and there, may be found

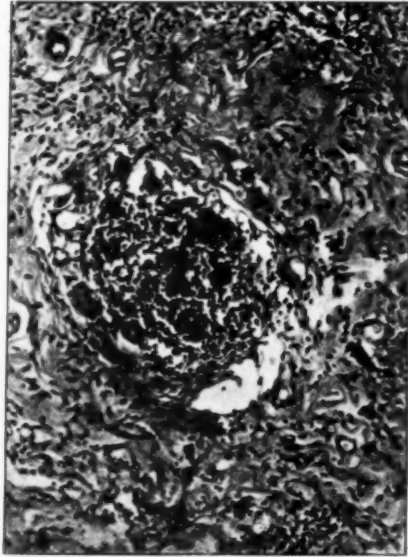


FIG. 3.

Section of thyroid gland from Case III. (Magnification 140.)

an atrophic acinus with a small lumen containing a little colloid. Parathyroid: Epithelial corpuscles are well seen, but there is also a marked increase of lymphoid tissue as described above in the thyroid gland. Some of the epithelial corpuscles seem to have hypertrophied, forming true acini with a comparatively wide lumen filled with a homogeneous colloid-like mass. Hypophysis cerebri (fig. 4). The pituitary body, although perhaps slightly hypertrophied, shows the usual structure of its cerebral and its glandular lobule. The chromophile cells are not markedly increased in number. The intermedial part is very richly vascularized, and seems to contain rather more colloid substance in its cysts than usual, the cysts being surrounded by small cubical and very chromophilous cells. Pancreas: Sections stained by hæmatoxylin-eosin exhibit irregular but fairly sharply limited clear patches to the naked eye, which seem in preference to have their seats in the neighbourhood of the principal fibrous and vascular septa. They correspond to foci of necrosis affecting the glandular tissue, whose cells, in those patches, are very faintly stained with a pale and often indistinct

nucleus. In the septa, and partly also infiltrating the necrosing parenchyma, there are numbers of diffuse hæmorrhages and coagulated masses of hæmorrhagic exudation. A diffuse and not very dense infiltration of round cells can be seen everywhere, but especially in the neighbourhood of the septa. In the fibrous tissue (which seems to be somewhat increased) many areas of a homogeneous appearance can be seen, staining deeply red with Van Gieson (connective tissue fibres in a state of hyaline degeneration). The muscularis of the larger ducts is thickened and partly in a condition of hyaline degeneration. With

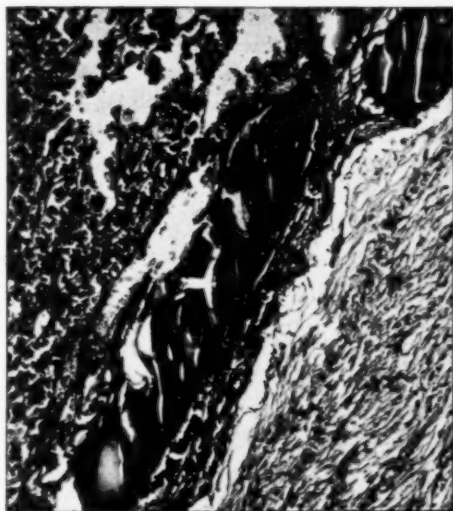


FIG. 4.

Section of the pituitary body of Case III. Between the light cerebral portion of the gland and the dark glandular portion is seen an abundance of colloid material, filling, as it were, a sinus. (Magnification 120.)

Gram's method a few diplococci (Gram-positive) can be seen lying free in the tissue. Beside these there are many saprophytes of all kinds which beyond doubt are of post-mortem origin. The liver shows nothing of importance excepting perhaps a slight increase of connective tissue. The heart and the spleen do not reveal any change. Kidneys: There is an intense hyperæmia, and here and there small capillary hæmorrhages can be seen. In some parts the epithelium appears to be

swollen up, but the nuclei are well seen. No increase of fibroid tissue.

(b) *Nervous System*.—It may be desirable to mention that the preparations stained with Weigert and Marchi methods did not reveal any degeneration of the myelin sheaths surrounding the nerve-fibres in this case, and the changes described relate, therefore, to the appearances presented by the various groups and systems of ganglion cells.

*Preparations of the Central Nervous System stained by Nissl and Bielschowski Methods.*

(1) *Cerebral Cortex*.—(a) *Anterior central convolution*: Nearly all Betz cells of the leg area show a certain amount of chromatolysis, but of a very varying degree of intensity. In the least affected cells the Nissl granules are still well shown, but the staining is more or less diffuse. Most of the cells, however, are in a more advanced stage of the chromatolytic change; the most frequent alteration met with being a central chromatolysis, the nucleus as a rule remaining still in the centre, but decreased in volume, and very often showing nothing more than the nucleolus (fig. 5). When the cell shows a total chromatolysis the nucleus is nearly always eccentric; the dendrites are missing or broken off. None of the cells are swollen up. In the advanced forms of chromatolysis a marked increase of yellow pigment is seen, which often occupies nearly the whole of the cell except the deeply stained periphery. There are only a very few completely disintegrated cells to be seen. The other cell layers of the motor cortex do not show any marked changes except a certain amount of hyperchromatosis (diffuse staining). The Bielschowski preparations show the fibrils generally well preserved. *Facial area, and tongue and larynx area*: These show about the same degree of chromatolysis of their Betz cells as the leg area.

(b) *Frontal cortex*: The small pyramidal cells of the frontal convolutions are mostly somewhat diffusely stained, but show neither definite chromatolysis nor any nuclear changes.

(c) *Broca's convolution*: There is some chromatolysis of the middle-sized pyramidal cells and of the cells of the multiform layer, but both of a slight degree only. (No total achromatosis.) We do not, however, consider these cortical cell changes sufficiently definite to be associated with any clinical symptoms manifested during life.

(2) *Cerebellum*.—The greater number of Purkinje's cells are unaffected; yet, among those apparently healthy cells, here and there a specimen in a more or less advanced stage of chromatolysis can be detected, but without ever showing nuclear eccentricity. By the Bielschowski method no definite changes are to be seen.

(3) *Medulla Oblongata (Medium Third)*.—The most marked changes occur in the medulla, where all the different ganglia, without exception, are affected, but in very varying degree of intensity. In the nucleus of the twelfth nerve the cells are generally only in the first stage of

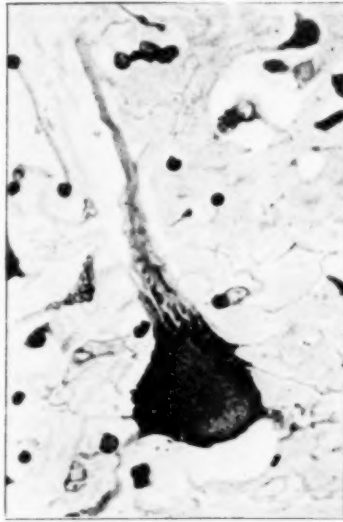


FIG. 5.

Section of motor cortex showing central chromatolysis of a Betz cell; the nucleus is indistinctly seen in the centre. Nissl stain. (Magnification 550.)

chromatolysis, showing no nuclear eccentricity, and no total loss of the Nissl granules. (Plate—3.) Here, too, the vagus system is by far the most severely affected, even more seriously than in the first case; in the dorsal vagus nucleus all the cells are throughout in a terminal stage of chromatolysis (fig. 6), most of them showing a total loss of chromatin and small oblong nuclei peripherally situated, or no nucleus at all. There are also numerous remains of completely disintegrated cells without nucleus or any other definite structure. No normal cells

can be detected. Likewise, in the nucleus of the solitary tract (Plate—2) all the cells are in advanced chromatolysis, and so they are in the nucleus ambiguus (Plate—1, *b*); yet, in the latter, the changes are not quite so grave as in the first, or in the dorsal nucleus of this case. The big “marginal cells” of the descending fifth root nucleus are in advanced chromatolysis. All other structures are less affected. The nuclei of the posterior columns exhibit very various degrees of chromatolysis of their cells, but only a few cells are in the terminal stage. Burdach's nucleus is more severely affected, except its external

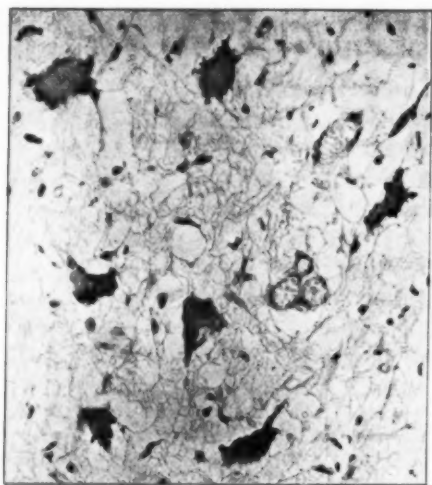


FIG. 6.

Cells of the vagus nucleus showing advanced central chromatolysis. Section of medulla oblongata of Case III; stained by Nissl method. (Magnification 390).

groups belonging to the cerebellum (Monakow's magno-cellular nucleus and nucleus restiformis, Gudden), in which the alterations are not so grave. The cells of the olivary bodies are mostly in advanced, but hardly ever total, chromatolysis, showing eccentric nuclei and an excess of yellowish pigment. The different association nuclei of the formatio reticularis are, generally speaking, affected in a moderate degree; there are (comparatively to other structures) numerous big multipolar cells with their Nissl granules well preserved.

(4) *Spinal Cord*.—In the cervical cord there is advanced chromato-



lysis of almost all the anterior horn cells without marked preference of any special group being noticeable; yet the middle cells and the fusiform cells of the posterior horns are less affected. In the dorsal cord the motor cells show generally the same degree of change as in the cervical region; the smaller cells of the lateral horns of the dorsal region, which give origin to the fine medullated (sympathetic) fibres, are especially affected. The cells of Clark's columns show throughout marked changes. In the lumbar cord the motor cells are generally rather less affected than in the higher levels of the cord.

(5) *Spinal Ganglia*.—All cells of the spinal ganglia which have been examined are somewhat more diffusely stained than usual. In

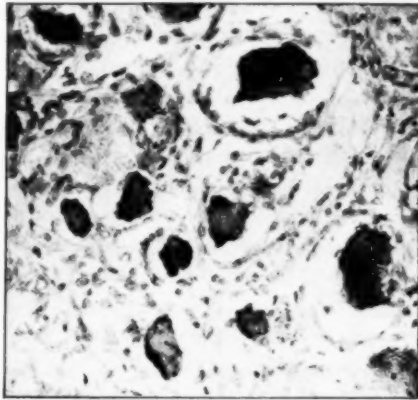


FIG. 7.

Section of dorsal posterior spinal ganglion, stained by Nissl method.  
(Magnification 250.)

the cervical ganglia only a very few cells are in a state of more advanced chromatolysis; if so, the capsular cells surrounding them are found slightly proliferating and filling up a part of the pericellular space. The smaller cells, which are supposed to have a relation to the sympathetic, are generally in a stage of hyperchromatosis or definite chromatolysis with eccentric nucleus. Numbers of cells show marked increase of yellow pigment. In the dorsal spinal ganglia a great number of the small cells show advanced chromatolysis with nuclear displacement, and more or less total absence of chromatin (fig. 7); most of them are shrunken, but the capsules do not show proliferation.

The big cells, too, are rather more affected than in the cervical ganglia, yet most of them have their nucleus in a central position.

(6) *Sympathetic Ganglion from the Lumbar Plexus* (Plate—4).—About two-thirds of the cells are in advanced chromatolysis; they are either faintly and diffusely stained with blue or hyperchromatic; a great number are shrunken and without nucleus or show an indistinct nucleus at their periphery. The interstitial connective tissue is very rich in nuclei. There is no proliferation of capsular cells.

#### (4) *Résumé and Conclusions from Case III.*

A woman, aged 37, of whose previous life not much is known, beyond the fact that she had been in bad health for some years, starts with an acute psychosis, with symptoms of both depression and mania, and corresponding, perhaps, to the clinical picture of a so-called "melancholia agitata." At the Claybury Asylum, where she was admitted, one of us (Dr. Mott) detected certain symptoms of myxœdema which led to a thyroid medication, but without any improvement. Three days before death the pulse suddenly grew extraordinarily slow, never rising above 48. The temperature became subnormal, and a complete inability to swallow food established itself, which was probably the cause of an inhalation broncho-pneumonia, that led to a rapidly fatal termination.

Therefore, here again, as in the two previous cases, we are dealing with a final and grave complication, whose symptoms strongly point to a severe functional disturbance of the autonomic bulbo-motor system, and in particular of the vagal centres. And again, as in the first case, we have found this presumption confirmed by the presence of even more advanced changes affecting the bulbar centres, especially the vagus nucleus, the dorsal vagus nucleus being almost in a state of disintegration.

Beyond these maximal and most striking changes in the vagus system there is a universal chromatolysis throughout the whole nervous system, sparing no structures entirely, but affecting them in very varied degree of intensity; for in the cerebellum, for example, only comparatively few cells are severely attacked, whilst the great majority seem to be quite healthy. Another fact worthy of special mention are the changes found in the spinal and sympathetic ganglia. It is noteworthy that the smaller sympathetic cells were the most affected in the spinal ganglia, possibly indicating, together with the

marked changes in the cells of the sympathetic ganglion, an elective affinity of the morbid process for the sympathetic and vagal systems. We shall refer to this interesting point later on.

The comparatively advanced cell changes found in the nervous system in this case seem to be correlated with the extreme atrophy of the glandular tissue and almost total absence of colloid substance in the thyroid. In respect to the acute hæmorrhagic pancreatitis, we are inclined to regard it merely as a complication secondary to the bronchopneumonic changes, with commencing gangrene in the lungs. It may be reasonably assumed that it was thus caused by a secondary infection by way of the diaphragmatic lymphatics. In favour of this view there are two facts: firstly, the presence of small Gram-positive diplococci in the pancreatic tissue; and secondly, the adherence of the posterior surface of the left lung to the pleura.

#### CRITICAL DISCUSSION AND SUMMARY.

Finally, it remains for us to discuss certain points which were found common to all the three cases which have been under consideration, for an analysis of those common points will perhaps enable us to arrive at a more definite conclusion regarding the pathogenetic connexion of the changes found in the nervous system with certain symptoms of the disease, and with the supposed morbid cause in general.

As we pointed out, the clinical aspect common to all three cases was a final and somewhat sudden aggravation of the morbid condition associated with grave and obvious symptoms of a disturbance in the autonomic vagal system of the bulb. Yet there is an interesting difference in respect to the special features of those vagal attacks in the three cases. In Case I, as will be remembered, we were dealing with a complete vago-glosso-pharyngeal paralysis, embracing as well the cardiotonic function, also the functions of swallowing and of articulate speech, whilst in the second case there was merely a certain degree of excitement of the first—the cardiotonic function. In the third case an obvious dissociation between the different vagal functions took place, the swallowing faculty being paralysed, whilst the cardiac apparatus still remained in a state of intense hyper-excitement (bradycardia).

The direct cause of these vagal crises was found in each case, as far as the medulla could be examined, to be an exceptionally grave chromatolysis throughout the cells of the different nuclei belonging to the bulbar, glosso-pharyngeus and vagus systems. Owing to the general

extent of these changes we can, of course, advance nothing in favour of a special localization of the different functions in question in one or other of these nuclei.

This partial bulbar paralysis confined especially to the vago-glossopharyngeus system may be a comparatively frequent complication in terminal myxœdema, owing to the fact that it occurred in two of the three cases here recorded, and an explanation may be asked, therefore, why the autonomic bulbar apparatus is so affected in myxœdema. We may advance two theories in explanation thereof: Either it may be due to a specific chemical affinity of the respective cells to a supposed myxœdematic toxin, or it may be the result of the earlier and more complete wearing out of these automatic centres, due to the fact that no rest is allowed to them, but that they have to go on functioning continually even under the most unfavourable conditions of general metabolism. Against the first supposition of a specific toxic affinity stands the fact that we are hardly entitled to speak of an elective lesion of the vagus system in our cases, since all the other structures, not only bulbar but also cortical and spinal, are likewise, though generally much less, affected. Further, we must emphasize here the point that the toxic nature of myxœdema is far from being an established fact, but, as Biedl<sup>1</sup> in his valuable lectures pointed out, both the clinical aspect and the favourable effect of thyroid medication of the disease clearly seem to indicate that the disease arises from a privation of certain substances necessary to general metabolism. We are therefore inclined to attribute the changes not to intoxication but rather to a chronic starvation of the neurones. Kocher, whose views regarding Graves's disease are well known, recently, in a discussion on the thyroid question,<sup>2</sup> expressed the opinion that both cretinism and myxœdema were the result of a hypo-function of the gland tissue.

Moreover, Asher and Flack<sup>3</sup> were able to show that the thyroid secretion acts directly upon the autonomic and the sympathetic nervous systems, the action upon the latter being more marked. Now in our third case we found, as will be remembered, the sympathetic cells not only in their own, but also in the spinal ganglia and the lateral horns of the spinal cord were severely affected by the chromatolysis, and it might

<sup>1</sup> Biedl, "Innere Sekretion," *Wien. Klinik.*, 1903, xxix, Heft. 10 u. 11, pp. 281-338.

<sup>2</sup> "83. Versammlung des ärztl. Centralvereins, 1912," *Correspondenzbl. f. Schweizer-Ärzte*, Basel, 1913, xliii, p. 298.

<sup>3</sup> Cit. from his volume on the same place.

be suggested that perhaps the deficiency of the normal stimulating action which the thyroid secretion exercises upon both the autonomic vagus and the sympathetic cells may account for the more marked changes presented by the cells in these centres.

A last fact to which we should like to call attention is the comparatively frequent coincidence of the myxœdematous syndrome with an acute psychosis, starting suddenly, as in our two last cases, and mostly having the character of a melancholia or a manic-depressive excitement. Cases, though rare, have been recorded of genuine manic-depressive insanity associated with myxœdema,<sup>1</sup> which seems to indicate that in this form of psychosis changes in the thyroid gland might be found. On the other hand, the connexion between the climacteric involution of the female sexual organs with both melancholia and myxœdema is well known, so that perhaps the primary cause of both affections may be dependent upon a departure from the normal balance of the hormones of the sexual and ductless glands.

#### FINAL RÉSUMÉ AND CONCLUSIONS.

(1) The changes in the nervous system in myxœdema consist in a general chromatolysis of the nerve cells of a subacute character and secondary to the disease.

(2) These changes, though general, are not of the same intensity throughout the different ganglionic structures, but they seem to affect in a particularly grave manner the autonomous bulbar-motor system (nuclei of the ninth and tenth nerves), and in second line, the cerebro-spinal motor neurons and the sympathetic system.

(3) Clinically, the affection of the vago-glosso-pharyngeal system can lead to severe vagal attacks, or, in advanced cases, to a fatal acute bulbar paralysis.

<sup>1</sup> Tomaschny, "Ueber myxœdematöse Hautveränderung als Parallelvorgang bei manisch-depressiver Psychose," *Neurol. Centralbl.*, Leipz., 1909, xxviii, p. 187.

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[We desire to acknowledge our indebtedness to Major Fink, I.M.S., for the coloured drawings.]

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OF THE  
ROYAL SOCIETY OF MEDICINE

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VOLUME THE SIXTH

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COMPRISING THE REPORT OF THE PROCEEDINGS FOR THE  
SESSION 1912-13

SURGICAL SECTION



LONDON  
LONGMANS, GREEN & CO., PATERNOSTER ROW  
1913



## Surgical Section.

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## Surgical Section.

October 8, 1912.

MR. G. H. MAKINS, C.B., President of the Section, in the Chair.

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### Injury of the Semilunar Cartilages.

By ALBERT J. WALTON, M.S.

SINCE Hey, in 1803, first described injury to the internal semilunar cartilage under the term "internal derangement of the knee-joint," many accounts of the condition have been given and much has been added to our knowledge of its pathology. The various lesions are, however, almost invariably described, both in modern text-books and in monographs, as being due to a sudden movement of internal rotation and abduction whilst the knee is in a position of semiflexion. An inability to follow this line of argument has led me to investigate the anatomical and clinical aspects of the parts of the knee-joint concerned in this lesion, and I believe that these investigations give the clue to the true method of production of such a lesion.

#### ANATOMY.

The anatomical structures of the knee-joint are fully described in all the text-books of anatomy, but it is necessary to discuss them briefly in order that the mechanism can be fully understood.

*The Semilunar Cartilages.*—The two semilunar cartilages probably represent the remains of a complete interarticular fibro-cartilage such as is found in the temporo-maxillary articulation. As may occasionally occur in this latter joint, a perforation appeared in the centre which gradually increased in size until only a circumferential band was left.

(a) *The Internal Cartilage.*—The internal cartilage forms a more open segment of a circle than the external. It will be noticed also that it is much narrower in front than behind (fig. 1), or in other words

that the articular surface of the tibia extends farther forwards in this position than on the external tuberosity, evidence that the pressure between the tibia and femur at this point is greatest internally. It is attached by its anterior horn to the upper surface of the non-articular surface of the tibia immediately in front of the attachment of the anterior crucial ligament. Internally it is fixed to the internal lateral ligament, excepting in front and behind, but in the latter

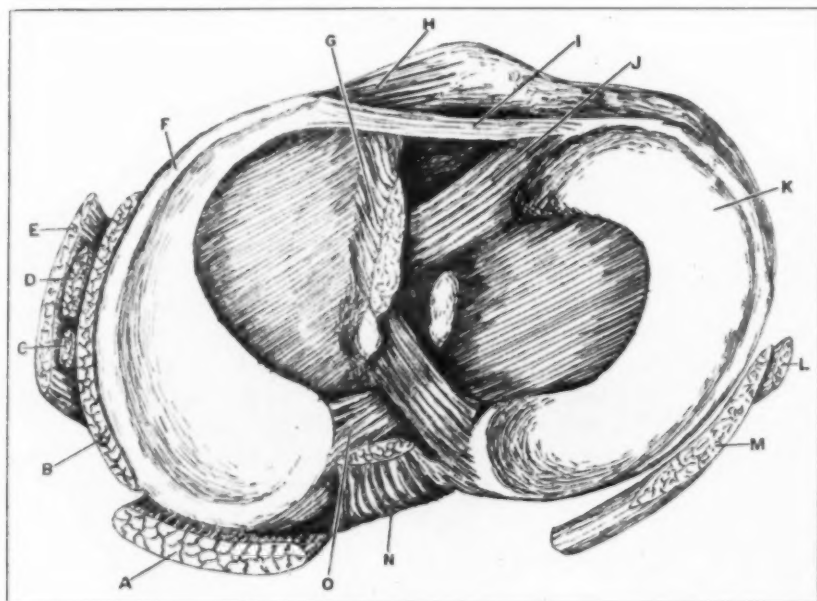


FIG. 1.

Relationships of the semilunar cartilages. **A**, semimembranosus; **B**, internal lateral ligament; **C**, semitendinosus; **D**, gracilis; **E**, sartorius; **F**, internal semilunar cartilage; **G**, anterior crucial ligament; **H**, anterior horn of internal cartilage; **I**, transverse ligament; **J**, anterior horn of external cartilage; **K**, external semilunar cartilage; **L**, external lateral ligament; **M**, tendon of popliteus; **N**, posterior crucial ligament; **O**, posterior horn of internal semilunar cartilage.

place it is protected by the semimembranosus tendon. At its inner edge it is bound down by the coronary ligament to the head of the tibia. It will thus be seen that the anterior third or so is free excepting for the attachment of the weak coronary ligament.

(b) *The External Cartilage.*—The external cartilage occupies a smaller area than the internal and its horns more closely approximate so that it forms almost a complete circle. It is attached by its anterior and posterior horns to the upper non-articular surface of the tibia close to the spine. In addition a strong slip, the ligament of Wrisberg, passes upwards from its posterior extremity to fuse with the posterior crucial ligament. Behind it is attached to the posterior ligament



FIG. 2.

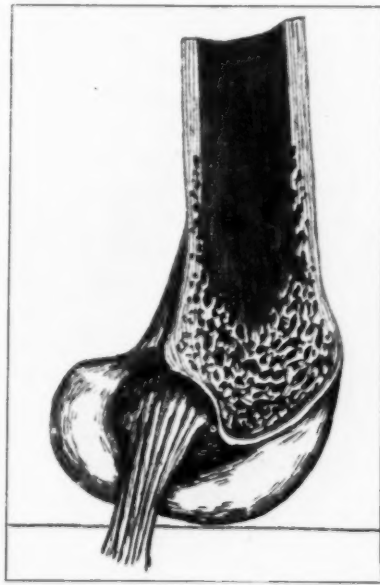


FIG. 3.

Fig. 2.—Attachment of anterior crucial ligament to inner surface of external condyle.

Fig. 3.—Attachment of posterior crucial ligament to outer surface of internal condyle.

of the joint and postero-externally is protected by the tendon of the popliteus. It is covered by, but is unattached to, the external lateral ligament. Anteriorly it is uncovered except by the thinned-out capsule. Like the internal cartilage it is attached to the head of the tibia by the coronary ligament. Its anterior end is therefore also but feebly bound down, and, as I shall show later, is even

more freely movable than the corresponding part of the internal cartilage.

*The Internal Lateral Ligament.*—This forms a wide strong band on the inner side of the joint, reaching as far forward as the junction of the posterior two-thirds with the anterior third of the internal semilunar cartilage. It is widest in the middle where the internal semilunar cartilage is firmly attached to it. Above it is fixed to the femur and below to the tibia, reaching rather lower than the level of the tuberosity of that bone. It is covered and augmented by the tendons of the gracilis, semitendinosus and sartorius muscles. Owing to the fact that the under surface of the condyle is flattened, the upper attachment of the ligament, which is placed behind the mid-point, will on extension of the knee be raised from the tibia. The ligament will therefore be tightened during this movement.

*The External Lateral Ligament.*—This is a rounded band attached to the outer surface of the capsule and free from the joint cavity. It is not attached to the external semilunar cartilage, being separated from it by the tendon of the popliteus. Like the internal lateral ligament, and for a similar reason, it is tightened during extension of the joint.

*The Anterior Crucial Ligament.*—The anterior crucial ligament is attached below to the tibia of the spine and above to the inner surface of the external condyle of the femur well behind the mean centre of rotation. Owing to this attachment (fig. 2) the ligament is tightened in full extension.

*The Posterior Crucial Ligament.*—This ligament is attached below to the tibia in the depressed area behind the spine, and above into the outer surface of the internal condyle of the femur. In the specimens I have dissected it was always inserted into the femur well behind the mean centre of rotation<sup>1</sup> (fig. 3) and not far forward as always stated; and thus, like the anterior ligament, was always

<sup>1</sup> The articular surface of the femur does not form the arc of a single circle, but may be regarded as being formed of two such arcs, one anterior and one posterior. These two arcs are joined below by an area which forms a flatter curve (fig. 21). The centre of the anterior arc will be at A, and that of the posterior at B. The lower end of the femur will not rotate around a fixed centre, but around one which, for this purpose, may be regarded as moving from B to A. The central point of this line (B—A) is the one I here call the mean centre of rotation, and it will be seen that any point situated on C—B will, on full extension—that is, when the articular surface (F E) comes into contact with the tibia—be carried farther away from the point D, which corresponds to the lower attachment of the posterior crucial ligament. On extreme flexion, when the femur is rotating around the point B, any point between C—B will again be raised—i.e., carried farther away from the point D.



tightened in full extension of the joint. At the same time the insertion into the femur is sufficiently far forward to lie in front of the centre of rotation of the posterior part of the articular surface, and thus the ligament is tightened again in extreme flexion.<sup>1</sup>

*Movements of the Femur upon the Tibia.*

If a dissected knee-joint be held in a position of flexion and be then gradually extended, the femur will be seen to roll upon the surface of the tibia, but the articular surface of the femur will at the same time be seen to slip backwards upon the tibia, that is to say, the

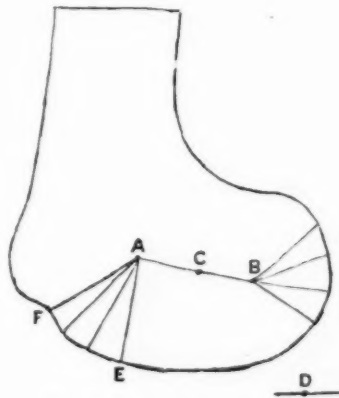


FIG. 21. (See footnote, p. 4.)

axis of rotation of the tibia upon the femur is not the articular surface of the femur, but a point some distance above it, corresponding to the upper attachments of the crucial and lateral ligaments.

As extension increases, both crucial and lateral ligaments are tightened, and thus the articular surfaces are slowly but very forcibly pulled together. Should any loose body be present within the joint the slipping movement of the femur upon the tibia would tend to draw it between the two bones where, with continued extension, it would be forcibly crushed between the slowly approximating bones.

At the end of extension both crucial ligaments are tightened, and since the posterior is attached to the internal condyle and the anterior

<sup>1</sup> Dissected specimens showing these attachments were exhibited at the meeting.

to the external condyle, therefore increased tension of these ligaments will give rise to two forces acting upon the femur in the line of the fibres of the ligaments and towards their tibial attachments. That is to say, a "couple" will be formed about the long axis of the femur (fig. 4) and thus this bone will be rotated in the direction of the arrows in the figure. If the femur be fixed the tibia will rotate only, of course, in the opposite direction—that is, outwards. Owing to this action, which is described as the screw action, a portion of the internal condyle of the femur more anterior than that of the external condyle comes into contact with the tibia, but it is to be noted that the extra portion of the articular surface of the femur found in this position is the effect

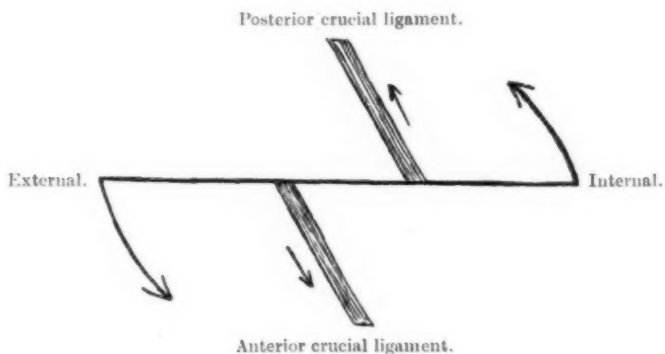


FIG. 4.

Action of the crucial ligaments in causing internal rotation of the femur at the end of extension.

and not the cause of this screw action. The true cause is the tension of the two tightened crucial ligaments. The dependence of this screw action upon the tension of the crucial ligaments is well seen in any specimen of the knee-joint from which all the ligaments with the exception of the crucials have been removed.<sup>1</sup> Owing to the screw action the movement of extension will be most marked on the inner side and anteriorly, and since extension is associated with tightening of the lateral and crucial ligaments, hence pressure between the two bones will be most marked in this area; in fact, there will be but little pressure on the external side. As already mentioned, this fact is also

<sup>1</sup> Such a specimen was shown at the meeting.

shown by the greater extension forward of the surface of the tibia which directly articulates with the femur, or, in other words, by the tapering of the semilunar cartilage in this position. When it is remembered that the semilunar cartilages are wedge-shaped on section, it will be seen that this forcible approximation of the tibia and femur will squeeze the cartilage from between them and force it inwards. In all my specimens this was a most notable factor<sup>1</sup> (fig. 5).

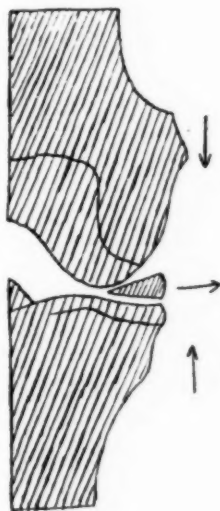


FIG. 5.

Showing how approximation of the tibia and femur leads to extrusion of the semilunar cartilage.

#### *Movements of the Semilunar Cartilages.*

If a fresh cartilage be removed from a subject in the post-mortem room it will be seen that its ends approximate and it forms a larger segment of a smaller circle than when in its original attached position. The change is most marked with the anterior end of the internal cartilage which, as already seen, is relatively narrow. It is due to the elasticity of the cartilage, and thus is not so well demonstrated in a dissecting room subject, although it may to a certain degree be regained by soaking the dried cartilage in water.

<sup>1</sup> Specimens showing this and the other movements described were exhibited.

*The Internal Cartilage.*—If the joint be examined in a position of full flexion it will be noticed that the tibia and femur are in contact behind, and that the wedge-shaped posterior end of the cartilage is to a certain extent pushed backwards in this position. But in front the thin anterior end of the cartilage owing (1) to its own elasticity, and (2) to the absence of pressure, tends to form an arc of a smaller circle, that is,

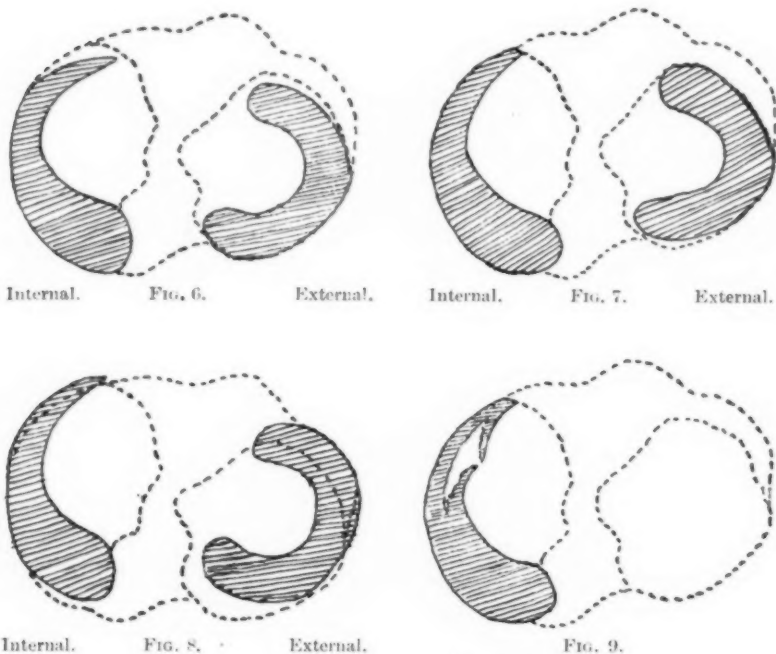


Fig. 6.—Position of the cartilages in full flexion.

Fig. 7.—Position of the cartilages in semiflexion.

Fig. 8.—Position of the cartilages in full extension.

Fig. 9.—Cartilage crushed by pressure between femur and tibia.

to pass further into the centre of the joint, being only restrained by the attachments of the coronary ligament and the anterior horn of the cartilage,<sup>1</sup> but in the living and to a less degree in the dead this movement does take place to an appreciable degree (fig. 6.) When, how-

<sup>1</sup> Specimens showing this and the other movements described were exhibited.

ever, the joint is brought into a position of semiflexion the anterior end of the cartilage, owing to the fact that pressure is being exerted upon it, passes inwards—i.e., out from the joint cavity until it occupies the margin of the articular surface (fig. 7). If the joint be now slowly extended the anterior end of the internal cartilage will be seen to project considerably beyond the articular surface of the tibia, and in fact to bulge over the edge (fig. 8). This is due to the fact that in this position the crucial and lateral ligaments are tightened, and thereby the articular areas of the femur and tibia are pulled together with con-

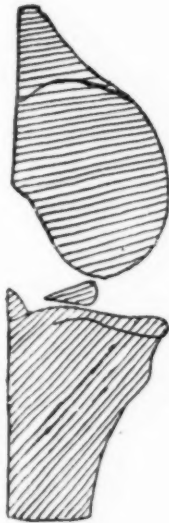


FIG. 10.

Fig. 10.—Cartilage lying abnormally near centre of joint in full flexion.

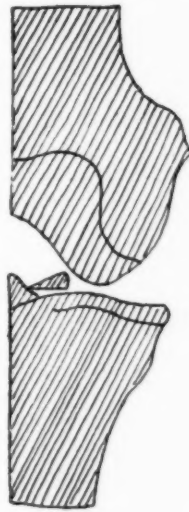


FIG. 11.

Fig. 11.—Cartilage pushed towards intercondylar space in full extension.

siderable force, and the wedge-shaped cartilage thus pushed inwards. It will be remembered that owing to the screw movement of the joint in the last stage of extension this pressure occurs almost wholly upon the anterior portion of the internal cartilage. The inward movement of the cartilage is only restrained by the anterior horn, the weak transverse ligament and the coronary ligament, for at this point the strong internal lateral ligament is absent. If, on the other hand, extension occurs so suddenly that the cartilage has not time to pass inwards, or

its movements, from any cause such as roughening of the femur or tibia, are hampered, it will then be caught between the two bones and be subjected to a very powerful crushing force which is liable to fracture the cartilage (fig. 9). During this movement the posterior end of the cartilage is free from pressure, the corresponding portions of the tibia and femur being separated; it tends therefore by its own elasticity to move towards the centre of the joint, but owing to its width in this position the movement is slight, and thus displacements or injury of this end would be expected to be rare. It will be seen that the portion of the femur in contact with the tibia forms, as it were, the rounded apex of a wedge on the inner face of which the semilunar cartilage lies, and it has already been explained how during extension the semilunar cartilage is pushed inwards along this face away from

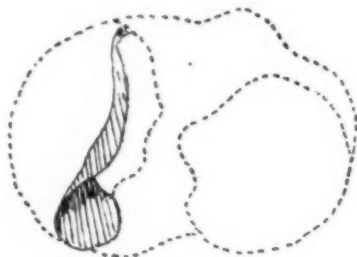


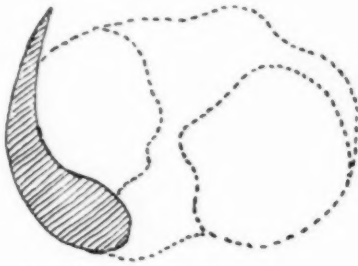
FIG. 12.

Cartilage lying in intercondylar space.

the centre of the joint. If, however, it should be farther out—i.e., nearer the centre of the joint—it would be pushed towards the intercondylar space by the sloping outer surface (figs. 10, 11 and 12). In no one of my specimens, however, could the *attached* cartilage be pushed in sufficiently far towards the centre of the joint to pass beyond the apex of the wedge of the internal condyle of the femur.

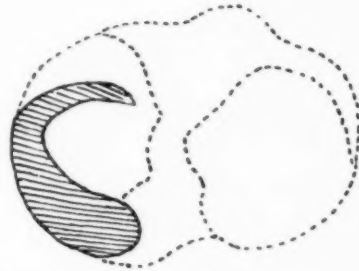
The above movements can be seen in all specimens, but they are best marked in fresh ones, and if such an one be taken powerful extension will be found to lead to marked internal bulging of the anterior end of the cartilage, and it can be well understood how sudden and excessive extension could separate its attachments. If now these attachments are artificially divided the anterior end of the cartilage will, on flexion, pass outwards—i.e., towards the centre of the joint—to an abnormal degree and will come to lie beneath the apex of the internal condyle

of the femur, so that on extension of the joint it will no longer be pushed inwards but will lie between the two bones, and, preventing their normal approximation, thus limit extension (figs. 13 and 14). The joint would thus be locked in a position of semiflexion, and the crucial and lateral ligaments being greatly stretched much pain would be caused in life. At the same time the cartilage would be compressed between the two bones and probably fractured, the fracture in this



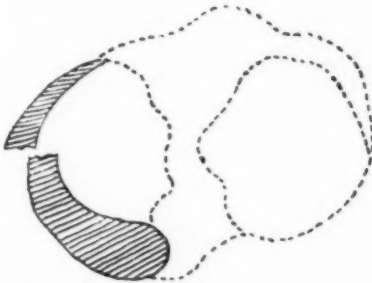
Internal.

FIG. 13.



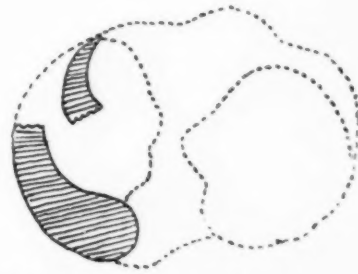
Internal.

FIG. 14.



Internal.

FIG. 15.



Internal.

FIG. 16.

Fig. 13.—Separation of anterior attachments of cartilage by forcible extension.

Fig. 14.—Separated anterior end of cartilage lying between femur and tibia on full flexion.

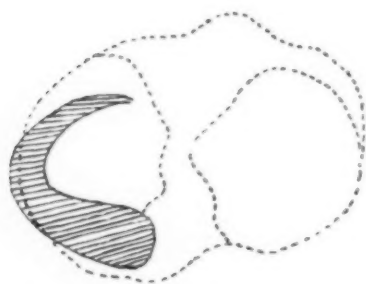
Fig. 15.—Fracture of anterior end of internal cartilage by forcible extension.

Fig. 16.—Fractured anterior end of cartilage lying between femur and tibia on full flexion.

case being secondary to the displacement. It is also easy to understand that, instead of its anterior attachments being torn through, the unprotected anterior part might be torn from the more fixed posterior part, and the position at which such a lesion would be most likely to



occur would be just in front of the internal lateral ligament, for here the fixed part is replaced by one which is more movable. If in the fresh specimen the cartilage be divided at this point the posterior extremity of the anterior end will curl outwards towards the centre of the joint (figs. 15 and 16) to lie again between the bones and cause locking of the joint in a position of semiflexion. If instead of dividing the internal cartilage it be separated from the internal lateral ligament and the coronary ligament be divided, the cartilage will, when the knee is flexed, tend to take up the position shown in fig. 17, and the anterior extremity can be readily pushed in sufficiently far to pass beyond the apex of the wedge of the internal condyle, so that on full extension it will be pushed outwards to the intercondylar space. When once this has happened the femur, during flexion, will, in its movement of rolling



Internal.

FIG. 17.

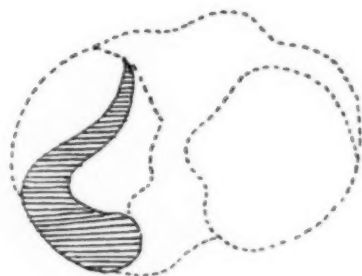


FIG. 18.

Fig. 17.—Position of separated cartilage on full flexion—first step.

Fig. 18.—Position of separated cartilage on full extension—second step.

backwards on the tibia, push bit by bit the rest of the cartilage into the intercondylar space. The stages of this movement are shown in figs. 10, 11, 17, 18, 19, and 12. One can believe that it would not be necessary for complete separation to be present for this to occur, for if the anterior end alone were freed and passed sufficiently far outwards, the rest of the cartilage would of necessity be pushed outwards—i.e., towards the centre of the joint—as flexion took place, and thus would be torn from its attachments to the internal lateral ligament. In no case was it possible by internally or externally rotating the femur, while the joint was semiflexed, to cause any inward or outward movement of the cartilage, even in those specimens where separation or fracture had been artificially produced.

*The External Cartilage.*—The movements of this cartilage are, on the whole, somewhat similar to those of the internal cartilage, but the differences which exist are of considerable importance. During full flexion the anterior part of the cartilage passes inwards towards the joint, but to a less degree than the internal one, because it is wider and thus less likely to undergo the changes in form due to its own elasticity. Hence one would expect that during sudden extension, even if roughening were present, this portion would be less likely to be caught between the tibia and femur (fig. 6). During semiflexion the anterior part of the cartilage begins to pass out from the joint, being pushed out from between the two bones in a manner identical with the internal, the posterior end at the same time passing somewhat into the joint (fig. 7).

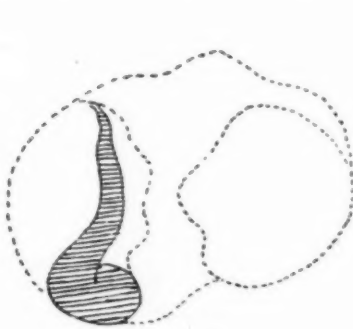


FIG. 19.

Fig. 19.—Position of separated cartilage on semiflexion—third step. For position in full flexion (fourth step) see fig. 12.



FIG. 20.

Fig. 20.—Position of internal cartilage on full flexion after complete separation laterally and in front.

During full extension there is, owing to the screw action, an entirely different movement; as the femur rotates inwards the external condyle is swung forwards and inwards as a whole—i.e., it slides forward upon the tibia. The cartilage goes with it, both anterior and posterior portions travelling forwards, so that in full extension the anterior part lies off the articular surface (fig. 8). But there is, on the external side, a relatively large non-articular area of the tibia anteriorly. On to this the cartilage passes and there remains, the femur moving over it. Thus, although the movement is more marked than in the case of the internal cartilage, there is here no pressure on the anterior part of the capsule

or pull upon the anterior attachments, and therefore separation of this portion of the capsule would be much less likely to occur. At the same time, the non-articular area of the tibia lies at a lower level than the articular, and thus the cartilage, once it has passed on to this area, would be relieved from pressure between the two bones, although, as previously described, there is, owing to the screw action, less pressure between the two bones on the outer than upon the inner side. For these reasons fracture of the cartilage would be unlikely.

A consideration of the anatomical factors leads, then, to the following conclusions :—

(1) There is a tendency to injury or displacement of the semilunar cartilages.

(2) This tendency is brought about by full extension and is increased with powerful or excessive extension.

(3) The tendency is much more marked at the anterior end of the internal cartilage because : (a) being narrower this portion of the cartilage more readily undergoes changes due to its own elasticity ; (b) owing to the screw action in full extension the compression force between the femur and tibia is much more marked here than elsewhere ; (c) the anterior end of the cartilage is unprotected and loosely attached.

(4) Either fractures or displacements of this portion of the cartilage may occur and are both easily explainable.

(5) There is no evidence of any tendency to fracture or displacement with any movement, provided the joint is not fully extended.

In other words, one would expect lesions of the anterior end of the internal semilunar cartilage to be much more common and to be the result of forcible or excessive extension.

It is now necessary to investigate the clinical aspects of this condition, to determine how far the facts obtained by an examination of the patient and of the lesions found at operation support the conclusions arrived at by a consideration of the anatomy of the joint.

#### POSITION OF THE LESION.

All investigators are agreed that the condition is much more common in the anterior part of the internal semilunar cartilage ; so constant is this that it is only necessary to quote a few figures. Rutherford Morison

[7] states that "of 100 cases, in 98 the internal and in two the external semilunar cartilage is fractured," but beyond stating that in some cases the lesion was so far back as to be in danger of being overlooked, as though suggesting that the anterior part is more commonly affected, he does not state the position of the lesion. In five of his six figures, however, the lesion is depicted in the anterior end. D'Arcy Power[8] in his series found 7 external and 83 internal. He states that if the cartilage is torn across the injury usually takes place in the anterior third. In the eleven years 1901-11 inclusive there were admitted to the surgical wards of the London Hospital 77 cases of injury to the semilunar cartilages; of these the internal was affected in 73, the external in 4 cases. Of the 73 internal the part affected was noted in 68. Of these the anterior third was alone affected in 62; the whole cartilage in 6 cases only. In not one case was a lesion of the posterior end alone noted, although, as Rutherford Morison [7] points out, lesions of the posterior end alone are very prone to be overlooked. The figures of Katzenstein [5] are very different from the above. He states that in his 83 cases the internal cartilage was affected twice as often as the external.

The explanation which is usually given for this marked preponderance of lesions of the internal cartilage is that its attachments are weak and thus much more likely to tear than those of the external cartilage, but, as already shown, in the normal joint the movements of the external cartilage are more marked than those of the internal, although it is subjected to less force. Godlee [3] has however, made a significant statement on this point. In referring to a case of displacement of the external cartilage into the intercondylar space he states that, "looked at from an anatomical point of view it would seem most likely that the external and not the internal fibro-cartilage should be the one to slip, for it will be remembered that the cartilages are retained in position chiefly by means of their attachment to the capsular ligaments of the joint." He then goes on to show that the external cartilage has a less extensive attachment to the capsule and expresses doubt as to whether the internal is really the more frequently separated. From the above figures there can, however, be no doubt that the internal is more frequently affected. The real explanation is that in spite of its greater mobility the external cartilage is subjected to less force than the internal owing to the presence of the screw action, and the movements all take place well within the capsule, so that there is relatively little pressure upon the anterior part of the capsule and thus less liability for its attachment to the cartilage to be

torn. In fact, the conditions as regards the position of the lesion found clinically are exactly what one would expect to find from an examination of the movements of the cartilage in fresh anatomical specimens.

#### NATURE OF THE LESION.

Of the 77 cases in the London Hospital series the nature of the lesion was noted in 52. In 14 of these the anterior end was torn from its attachments as in figs. 13 and 14, the free extremity in several of them having become thickened and polypoid. In this series it was the most common type of lesion. Rutherford Morison [7] has pointed out, however, that separation by itself is a rare lesion, being more commonly associated with a longitudinal fracture, and since such a fracture may be incomplete and only visible from the under surface, as in the following case, it is possible that many cases previously recorded as simple displacements may have been associated with a fracture.

B. M., aged 20, was admitted to the Seamen's Hospital, Greenwich, on September 27, 1911. He stated that five days previously he was thrown out of his bunk while at sea, his right foot being forcibly everted whilst his leg was extended. He felt sudden pain in the knee which caused him to bend it, after which he was unable to straighten it. The knee had remained swollen and painful until he was admitted to hospital. The right knee was found to be slightly flexed, attempts at extension causing considerable pain, which was referred to the anterior part of the inner side of the joint. There was an increase of fluid in the joint. A localized area of tenderness was discernible over the anterior end of the internal cartilage, and here a small swelling was felt which was present on extension but disappeared on flexion. A week later I opened the joint by a vertical and slightly curved incision over the anterior end of the cartilage, which was found to be quite free as far back as the anterior border of the internal lateral ligament. At this point the cartilage was divided with a tenotomy knife and the anterior part removed. The joint was then closed. The under surface of the removed portion of the cartilage showed three small incomplete fractures, which were invisible when the cartilage was in position. Four weeks later he was using the leg in perfect comfort.

The fact that such fractures may be incomplete and occur on the under surface of the cartilage would be a point in favour of the operation suggested by Barker [1] of opening the joint below the semilunar cartilage.

The second most common lesion in this series was a transverse fracture. Rutherford Morison [7] first pointed out that fractures were more common than displacements. This is borne out by the present

series. Of the 52 cases noted, 28 showed some form of fracture, but whereas in his series a longitudinal fracture was the most common event, in this series a transverse fracture was the more frequent, 13 of the cases showing this lesion. But, as already mentioned, longitudinal fractures are at times very difficult to recognize and it is possible that in some of the earlier cases such a lesion was overlooked. In every case of transverse fracture it is noted that the injury was situated at about the junction of the anterior and middle thirds, that is, in front of the firm attachment to the internal lateral ligament. These two types of lesion are the ones in which the cartilage can be felt, for when the joint is extended without locking the anterior part is expressed. In this series the cartilage could be felt 17 times, 10 were transverse fractures and 7 anterior displacements.

Anatomical specimens have already shown us that a longitudinal fracture may occur either as a primary lesion or be secondary to a displacement of the anterior extremity. We should therefore expect such a lesion to be common. In fact, Rutherford Morison states that "since the fact that fracture of the cartilage was the true pathology occurred to me, no case of my own or of my colleagues has been seen to refute this view." In this series a simple longitudinal fracture was noted in 11 cases, combined with a displacement of the anterior extremity in 2 cases and combined with a displacement of the whole cartilage in 2 cases. The extent of the fracture may be very variable. In the minor degrees there is simply a small fissure generally nearer the free edge of the cartilage. At the other extreme are seen cases where the fracture extends nearly the whole length of the cartilage, so that the inner strip is widely separated from the outer. If the fracture be limited to one portion of the cartilage it is always the anterior third that is affected, as in the following case:—

H. C., aged 22, was admitted to the Seamen's Hospital on September 22, 1911. He stated that two years ago he noticed pain in the right knee after returning from roller-skating, although he had no knowledge of any injury to the joint. Owing to the pain he was in bed for two days, but the joint remained slightly swollen for six months. It then recovered perfectly, so that he played football in the 1910-11 season. On September 16, whilst running over rough ground, his foot slipped and was forcibly everted. This caused sudden severe pain on the inner side of the knee, but he was able to walk home, a distance of half a mile, the joint not being locked. The knee had remained painful and swollen since. The right knee was found to be somewhat swollen and was kept in the semiflexed position. Attempts at extension caused pain and, at times, a definite click on the inner side of the joint. An area corresponding to the

anterior part of the internal cartilage was tender on pressure, but no swelling could be felt here. A week later I opened the joint and found the anterior portion of the anterior cartilage split longitudinally for a distance of 1 in. The attachments of the anterior third of the cartilage were divided with a tenotomy knife and it was removed. The joint was then closed. Three weeks later he was walking freely on the leg with no symptoms.

Of the eleven cases in this series showing longitudinal fractures, three extended the whole length of the cartilage, in the other eight the lesion was limited to the anterior third, that is to say, it always commenced in the anterior third, and if it increased passed gradually backwards.

A rarer type of lesion is one in which the cartilage remains attached by its anterior and posterior extremities, but is separated at the circumference. This separation may be limited to a small area or the whole cartilage may be detached, in which case it usually passes outwards, to lie curled up in the intercondylar space. I believe that these conditions are but degrees in one type of lesion, and therefore include them here together. There were in this present series five examples of each lesion. In the first case, that of partial separation, the condition was limited to that part of the cartilage in front of the internal lateral ligament in four. In the fifth case, where the external cartilage was affected, the anterior portion was also at fault.

If the cartilage be completely separated circumferentially, but its anterior and posterior attachments remain, it will lie in the intercondylar notch. The mechanism by which this takes place has been explained by the anatomical specimens (figs. 17, 10, 11, 12, 18, and 19). In some rare cases the anterior attachments may also be torn, so that the cartilage is attached by its posterior horn alone. In such a case the cartilage will be found rolled on itself on the posterior part of the upper surface of the tibia, as in a case recorded by Katzenstein [5]. In the anatomical specimen represented in fig. 20 the cartilage has been freed from its attachments in this manner, and the method of displacement of the cartilage is easily seen. It will be understood from an examination of figs. 17, 18 and 19 how, if the anterior end is free, it will pass back with the rest of the cartilage on gradual flexion until the whole cartilage lies posterior.

The nature of the lesions found clinically is therefore identical with those which can be easily produced in anatomical specimens.



## METHOD OF PRODUCTION.

When the mechanism of the injury is inquired into from the clinical aspect there appears a marked discrepancy between it and the anatomical evidence. In all the specimens I have examined, which are represented in the diagrams, there was not the slightest evidence of any force which could lead to injury of the internal cartilage whilst the knee was in a flexed or semiflexed position. It is true that in the semiflexed position with the tibia everted, the anterior end of the cartilage passes farthest into the joint cavity, for in this position the tibia and femur are most widely separated. But even if the anterior extremity passed sufficiently far in to become separated from the capsule, which I cannot believe possible, there is still wanting an explanation of the common lesions of transverse and longitudinal fracture. On the other hand, forcible extension is capable of most faithfully reproducing every form of lesion that is clinically met with, but it must be remembered here that extension terminates by an outward rotation of the tibia upon the femur, so that if the leg be extended and the foot be forcibly rotated out, there is but the continuation of one movement, that is, extreme extension.

Clinical evidence, however, has always been unanimous in showing that the lesions arise whilst the leg is in a position of semiflexion. So constant is this that it is unnecessary to give references. I may simply state that in every account in the literature that I have been able to examine the same statement is made. Most writers believe that with this the tibia is everted, but Barker [1] states that in his cases the tibia and foot were generally inverted. He gives a clear account of the movements of the cartilage as seen in the living body at operation, and describes how during flexion the anterior end of the cartilage passes by its own elasticity towards the centre of the joint and during extension is expressed from between the two bones. But in spite of this he believes that the condition arises with the leg in a position of flexion.

How, then, are these divergent pieces of evidence to be brought into line? The first point to question is the history of the accident as given by the patient. The usual statement made is that while undertaking some form of exercise he felt sudden pain in the knee which caused him to fall, and on attempting to rise the knee was found to be fixed in a flexed position, from which he not unnaturally assumes that the joint was flexed at the time of the accident. It is, however, possible that the flexion might have been secondary and have been brought about to relieve the pain caused by the injury to the cartilage,

and being almost reflex be unnoticed by the patient. It is therefore safer to inquire into the nature of the exercise and deduce from this, if possible, the movement of the affected leg.

Of the 73 cases in this series there was a definite history in 65. The greatest number, 25, were caused at football. In two of these the patient kicked at the ball and missed it. Here there is a clear history of hyperextension. In 21, whilst running the foot slipped on the ground and was forcibly everted. Now the position in which the foot would slip would be either when the weight of the body is first thrown upon it or with the forcible thrust of the back leg at the end of its stroke, that is, in either case with the leg fully extended. In the remaining 2 cases of this group a second player fell across the patient's outstretched knee, hyper-extending it. Of those occurring apart from football, 15 arose from the foot twisting outwards whilst walking over rough ground, and 5 whilst running under similar conditions. The mechanism here would be similar to that of the last group of cases. In 11 others the patient fell from a height, 3 of them whilst stepping from a train on to a platform which was lower than usual. In these 3 the position of extension is clear. The others are explained simply by supposing that the body-weight fell forwards after the feet struck the ground, although the history of such a condition is of course not clear. In 4 cases the condition arose whilst jumping. Here again the sudden forcible extension at the moment of the take-off is evident. Two were boxing and one wrestling. In both the boxers the affected leg was the left, this being in front and extended, the body was suddenly rotated to the right to avoid a blow, the screw action of hyper-extension being thereby exaggerated. In this connexion it is interesting to note that cases are reported in golfers. I have not personally met with such, but I believe the explanation will be that in the upstroke of the "drive" the left leg has been kept extended instead of partly flexed, the rotation of the body thereby causing the increased screw action. One case arose whilst throwing a cricket ball, the action here being similar to the last. In the remaining case the patient was rising suddenly from a stooping position, the leg being thereby extended.

In some cases there is a history of several accidents, the first being associated only with pain and swelling without locking. The symptoms are entirely recovered from, it being only after the second or third accident that the complete clinical picture arises. This would point to the injury being incomplete at first but gradually increasing with the subsequent accidents. In this series there were 7 cases showing such

previous slight accidents followed by some pain and swelling, which after a relatively short time cleared up entirely and was associated with locking. A later accident, sometimes the fourth or fifth, was associated with more severe symptoms and was followed by a condition of instability of the joint.

A consideration of the ætiological factors may also throw some light upon the subject. If the condition were simply dependent upon the cartilage in its anterior part slipping between the two bones whilst the tibia were flexed, abducted and externally rotated the condition would be equally common among males and females, for no excessive muscular action would be required. Barker [1], indeed, found that such was the case in his series. But in this present series, which, taken wholly from a large general hospital, I believe to more accurately represent the true state of affairs, there is a marked discrepancy between the two sexes. Of the 73 cases of lesion of the internal cartilage only 8 were females. That is a ratio of 8 males to 1 female which points to excessive muscular action, such as is present in hyper-extension, being an active factor.

The age-frequency, again, shows that the lesions are much more common at those ages in which excessive muscular action is indulged in. The youngest was aged 13, the oldest 44. The following table represents the age-frequency in the 73 cases of lesion of the internal cartilage.

| Age         |     |     |     |     |     | Number of cases |
|-------------|-----|-----|-----|-----|-----|-----------------|
| 11—15 years | ... | ... | ... | ... | ... | 2               |
| 16—20 "     | ... | ... | ... | ... | ... | 12              |
| 21—25 "     | ... | ... | ... | ... | ... | 25              |
| 26—30 "     | ... | ... | ... | ... | ... | 14              |
| 31—35 "     | ... | ... | ... | ... | ... | 7               |
| 36—40 "     | ... | ... | ... | ... | ... | 8               |
| 41—45 "     | ... | ... | ... | ... | ... | 5               |

It is sometimes stated [6] that the production by sudden rotation in a position of semiflexion explains the greater frequency with which the left knee is affected, most sudden movements being made from left to right. In this series, however, the right side was rather more frequently affected, 45 were right-sided, 42 left-sided, figures which are in close agreement with those of Rutherford Morison [7], who in his private and hospital cases combined found 80 right-sided and 63 left-sided. This is in accordance with the view that the lesion is due to excessive muscular action or forcible hyper-extension.

Forcible hyper-extension, with its accompanying external rotation of the tibia, would tend to throw considerable strain upon the crucial

ligaments, and it is here interesting to note that Sir William Bennett [2] states that "the commonest, perhaps, of all intra-articular lesions, although it is one which has not received much attention in cases of this kind, is, I believe, more or less laceration of one or both crucial ligaments." R. Jones [4], on the other hand, states that "the displacement or fracture of the internal semilunar cartilage can only take place when the internal lateral ligament is stretched or ruptured." In this present series of cases there was, however, in no case any evidence of rupture of the internal lateral ligament, a lesion which could hardly have been overlooked at operation.

Of the four cases of lesion of the external cartilage it is to be noted that in three the anterior extremity of the cartilage was alone affected, whilst in the fourth case the whole cartilage was displaced inwards towards the intercondylar space. In two cases there was a history of forcible extension, jumping in a gymnasium, whilst in the other two there was a history of a severe blow on the anterior and outer surface of the joint, this probably tending to hyper-extend the joint. The cases are too few for any accurate deductions, but so far as they go they seem to point to a mechanism similar to that giving rise to injury of the internal cartilage.

An investigation of the clinical factors gives rise, therefore, to the following conclusions:—

- (1) The lesions present are identical in nature and position with those which can be artificially produced by hyper-extension and its terminal screw action.
- (2) The history when carefully investigated gives evidence of hyper-extension as a cause.
- (3) The aetiological factors are in favour of the same view.

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### **Injuries to the Semilunar Cartilages: a Personal Experience of 449 Cases of Operation.**

By ALBERT M. MARTIN, B.S. (Newcastle).

DURING the past ten or eleven years I have been much interested in the subject of injuries to the semilunar cartilages, and inasmuch as this class of case is extremely common in the northern counties of England I have had ample opportunity of studying it.

On looking through the notes of both my hospital and private patients I find that, during the period between the end of the year 1900 and the end of the year 1911, I have operated upon 449 cases (413 hospital and 36 private) diagnosed as suffering from injury to the semilunar cartilages. All the patients made good recoveries, and in no case was there any resulting joint infection, or any interference with the after-stability of the joint. In a few cases—and this applied particularly to those in which no definite pathology was found at the operation—complaint was made that the symptoms had not been relieved; otherwise the results were all that could be desired.

One of the commonest industries in Northumberland and Durham, if not the commonest, is coal-mining, and this industry far outnumbers all the rest in the district in supplying the vast majority of sufferers from this accident. The reason why this is so is not far to seek. The coal-miner, owing to the lowness of the seam at which he is hewing, performs his work with his knees more or less flexed. In this position, owing to relaxation of the internal, posterior, and anterior crucial ligaments, a certain amount of rotation and lateral mobility between the upper end of the tibia and the lower end of the femur is permitted, and it therefore follows that if, while the knee is in the flexed position, a forcible twist or wrench takes place—such for instance as might happen in throwing coal, while in a squatting position, when the body is swung round too far—one or other knee is twisted, and the cartilage may be torn. Where the accident does happen the cartilage, nipped between the condyle of the femur and the upper end of the tibia, is forcibly dragged towards the centre of joint, and either split more or less in a longitudinal manner, or its free edge torn or frayed.

I have been unable to satisfy myself that there is ever a true detachment, as in every case observed, even where the split is very

near the attached margin, a narrow rim of cartilage still retains its normal position. I would here wish to emphasize that where a proper diagnosis has been made, the injury is always in the nature of a tear or split, and where such is not found the probability is that a wrong diagnosis has been made, some other structure having been injured, probably the internal lateral ligament. In the present series of cases 95·5 per cent. of them showed definite splits or tears, so that only in 4·5 per cent. was there no definite pathology. These latter, I presume, are what are termed "loose" in the various text-books.

As I have before stated, coal-miners are the most frequent sufferers from torn semilunar cartilage, and in the present series, out of 449 cases 282 occurred in miners while following their employment. This gives a percentage of 62·8.

Football players are also very liable to the accident, and when we remember that in football the running is, as a rule, not straight, but consists rather of dodging, twisting and swerving, one is not altogether surprised. I am also inclined to think that the long leather studs in the boots, fixing the foot in the ground during swerving or dodging, while the body momentum goes on, are often the primary cause. Out of my 449 cases the accident occurred, in the first instance, while playing football eighty-one times. This gives a percentage of 18. It will be noted, therefore, that the mining occupation and football playing are responsible for 80·8 per cent. of the injury. Other forms of sport supply 2 per cent.

The internal semilunar cartilage is very much more often injured than the external. In the present series of cases the former shows a percentage of 92, while the latter shows a percentage of 8. For a long time I was under the impression that the reason the internal semilunar cartilage was more often torn than the external, was the nature of the accident. It seemed to me that an inward twist, where the femur is rotated inwards and separation of the joint surfaces takes place at the inner side, was the factor which would cause tearing of the internal semilunar cartilage. I found, however, that this was not always so, a great many of the patients being positive in asserting that the knee was twisted outwards. I am therefore driven to the conclusion that both an inward and an outward twist will cause rupture of the inner cartilage. Perhaps the reason is to be found in the anatomical conditions. We know that while the internal semilunar cartilage has a close connexion with the capsule and internal lateral ligament, the attachment of the external semilunar cartilage to



the capsule is looser, and it has no connexion with the external lateral ligament. Under these conditions, supposing the external semilunar cartilage was nipped between the external condyle and the upper surface of the external tuberosity of the tibia, and thrust towards the centre of the joint, and bearing in mind the limited lateral excursion of the femur which would be permitted, a tear of the cartilage would not be likely to take place, but rather, in the majority of cases, at the most, stretching of its connexions. On the other hand, if the internal cartilage be nipped between the internal condyle and inner tuberosity of the tibia, and dragged towards the centre of the joint, considering its much closer connexion, a split or tear would often result.

The right knee is slightly more frequently affected than the left, the percentage of the one being 53·3 and of the other 46·7. In the case of six patients both internal cartilages were removed, in one case at the same operation, and in the others with an interval of from six weeks to five and a half years. In one patient both external cartilages were removed with an interval of one year. In two cases, in both of which the internal semilunar cartilage was diagnosed as torn, on operation these were found normal. An incision was therefore made on the outer side of the joint, and the external cartilages, much torn and mutilated, were removed. These two cases show that sometimes it is impossible to diagnose whether, in the case of an injured knee, the internal or the external semilunar cartilage is at fault. In two cases from the same knee both semilunar cartilages were removed, in the former with eight months', and in the latter with eleven months', interval between the operations. In two cases where, after operation for injury to the internal semilunar cartilage, the symptoms were not relieved, the joint was again opened. The portion of cartilage left behind after the previous operation was found to be torn and was removed with complete relief of symptoms.

Many types of torn semilunar cartilage are met with, and examples of these I will show you. In the first place there is the simple longitudinal split, varying as regards its position to its attached border, being sometimes quite close to this and sometimes quite near to the free edge. When the accident is recent the edges of the tear show roughness and are often blood-stained, while the joint cavity itself contains blood-stained synovial fluid. Where the primary accident occurred some weeks or months previously the edges of the split are rounded and smooth, and in some cases at the ends of the split some cicatrization may be noticed. The split does not extend straight



through the substance of the cartilage, but rather in an oblique manner from near its circumferential attachment downwards and towards the centre of the joint, so that on the upper surface of the cartilage the tear is near the outer circumference; on the under surface it shows nearer the free edge.

In some cases, on opening the joint the detached portion is seen lying in its normal position, and if a careful search be not made it might easily be overlooked. Again, in other joints the detached piece will be found curled up between the condyles, and practically only attached by its anterior and posterior ends. Sometimes the split is in the posterior part, and cannot be demonstrated until the anterior attachment of the semilunar cartilage is divided and strongly pulled upon, when the detached portion snaps forward. In one case, after a long search I found the detached portion lying stretched round the condyle.

In another type the tear extends from some point in the free border, across the breadth of the cartilage for a variable distance, and then either forwards or backwards. In the former case the detached portion may form a pedunculated piece, which, previous to operation, may be felt moving in front of the internal condyle. In another type the free border is the part that has been torn, forming a small pedunculated disk with round edges, and in some of these showing where it hinges over the free margin of the still attached cartilage. This pedunculated disk may form one of the varieties of loose bodies, in consequence of becoming completely separated as a result of being frequently ground between the joint surfaces. In still another type there is a more or less horizontal split through the thickness of the cartilage, the undermost piece being liable to engage between the joint surfaces and so cause symptoms. This type may be combined with the simple longitudinal split. In a minority of cases the injured cartilage is mutilated beyond all recognition.

The bulk of the sufferers from torn semilunar cartilage give a very typical history, and I would here emphasize that in the majority of cases we have to diagnose the condition from what we are told. It may be that when you first see the patient the primary tear occurred months or years previously, and the subsequent attacks of "something going wrong with the joint" have been comparatively slight, consisting perhaps of little more than experiencing a click or a snap at the inner side of the knee, with pain in the same situation. He then finds that momentarily the joint locks—i.e., he is unable to extend it completely; then suddenly, after moving his knee himself or somebody moving it for

him, another click or snap is experienced, and full power of movement is again regained. Attacks such as these occur more or less frequently, and at various intervals after the primary tear, and are often followed by no effusion, the only symptom remaining being a tender point at the inner or outer side of the patella somewhere in the line of the articulation, according as it is the internal or external cartilage that is injured. These subsequent attacks are often determined by very slight causes, such as catching the bedclothes with the toes, stepping on irregular ground, or rising from the squatting position. When, however, they do occur they render the limb perfectly helpless for a time, and may happen at very awkward moments, as, for example, when crossing in front of a tram or a motor car. One of my patients sustained a severe punctured wound of his palm in consequence of spiking his hand on some iron rails, which he had attempted to grasp in order to prevent himself falling.

When the primary tear takes place the symptoms are much more severe, and are often as follows. In consequence of a severe wrench or twist the patient is suddenly seized with severe pain. The pain is at first often felt over the whole joint, later becoming localized at the inner or outer side, and is frequently so bad as to cause faintness and vomiting. At the same time a click or snap is felt, or a feeling of something slipping. If running he falls to the ground, and finds he is unable to extend the knee completely. Often some witness of the accident at once practises flexion and extension movements, another click or slip is felt, and the joint is then found to be capable of complete extension. In a few hours swelling occurs, the result of effusion in the joint, and this, in consequence of rest, disappears in the course of two or three weeks. In some cases the inability to extend persists for a week or more, and in others only disappears when an anæsthetic is given and certain manipulative procedures are carried out or the offending cartilage is removed. For some weeks after the accident, and after all swelling has disappeared, a tender point persists at the inner or outer side of the patella, according as the internal or external cartilage has been torn.

In deciding upon a line of treatment, the question arises as to whether it is necessary for the patient to have a perfectly sound joint or not. If he is engaged in manual labour the answer must be in the affirmative, and in the absence of any contra-indication, such as inter-current disease, operation is demanded. This decision must also apply to active men and women who are still wishful to spend their leisure in open-air sports such as football, cricket, hockey, shooting and riding.

I am aware, of course, that in some of these cases the application of a knee-splint, which while permitting flexion and extension, prevents rotary and lateral movements, may prevent the joint "going wrong," but for such a splint to be really effective it must be somewhat heavy and cumbersome, and this the patients will not wear as a rule, or at any rate, discard it after using it for a short time. I am afraid I am very sceptical as regards the result of treatment by prolonged rest in the case of a primary tear bringing about a cure, in view of the conditions found in operated cases.

Where the inability completely to extend the joint persists operation is certainly demanded. Even where it is hoped that reduction under an anaesthetic may occur, this procedure should not be attempted unless the joint has been thoroughly prepared, so that in the event of failure an open operation may be performed. If operation be decided upon, the question next arises as to which is the best time to operate. Personally, I see no objection against doing this after the first week or ten days following the primary accident. I choose this time because I judge the devitalizing effect of the trauma will by then have passed away, and attempts at repair have started. Where operation is decided upon in consequence of repeated attacks of locking, it does not matter when the operation is performed (although personally I again prefer to wait until a week or ten days has passed), as the effect of the last attack will probably be so slight as not to lower the joint resistance.

Previous to, and during operation, the most rigid antiseptic precautions are called for. For thirty-six hours I keep the patient in bed, and at the beginning of this period the skin of the thigh and leg is shaved, thoroughly washed with spirit, soap and water, then with turpentine, and finally with methylated spirit. A compress wrung out of 1 in 1,000 perchloride of mercury solution is then applied around the limb, extending from the middle of the thigh to the middle of the leg. This is covered with mackintosh and secured by a bandage. The same procedure is carried out twenty-four hours later, and then, when the patient is on the operating table, and after a tourniquet is applied round the thigh, the knee is strongly flexed and kept in this position by my assistant. Before making the incision the operation area is thoroughly washed with a solution of 1 in 20 carbolic acid.

The incision I use is a transverse one, extending, in the case of the internal cartilage, from the inner border of the patellar tendon, backwards for about 2 in. in the line of the articulation. This incision, I consider, gives the best exposure, and if the internal lateral ligament be

not cut across there is no interference with the after-stability of the joint. After the skin is divided a strong aponeurosis is exposed, and is also divided in the length of the incision. The capsule with underlying synovial membrane is then opened, and the interior of the joint exposed. Then, in the great majority of cases, the tear or split will be quickly recognized, especially where it involves the anterior part of the cartilage, or where there is marked displacement of the torn portion. If after careful scrutiny nothing pathological is discovered, I divide the anterior attachment of the semilunar cartilage, seize it with strong toothed forceps, and drag it forwards. If there be a posterior split the detached portion will suddenly snap forwards between the condyles and tuberosity. This snapping forwards is what actually happens during an attack, and if witnessed it can be readily appreciated what a shock it will be to the patient. In every case I remove not only the detached piece, but endeavour to ablate the portion still retaining its normal attachment, and since doing this have had no patient returning with recurrence of symptoms. After the cartilage is removed the capsule and synovial membrane are sutured in one layer with catgut. The aponeurosis is similarly dealt with, and the skin incision is closed with a subcuticular suture of silkworm gut. An antiseptic dressing is then applied, with a thick layer of wood-wool wadding, and secured by a domett bandage firmly applied. No splint is used, and the patient is told to commence to move his knee as soon as he can.

After the operation a rise in temperature for the first two nights to 99° or 100° F. is commonly met with, but this need cause no alarm. Again, for the first forty-eight hours a great deal of pain may be complained of, necessitating one or two hypodermic injections of morphia. Otherwise the convalescence of the patient is perfectly straightforward, and at the end of a week the subcuticular suture is removed. After this is done a light dry dressing is applied, and my infirm patients are discharged, as a rule, on the tenth day, being then able to carry out full movements of the joint. In the case of one patient convalescence was disturbed by an attack of acute gangrenous appendicitis, for which operation was promptly performed eleven days after the cartilage had been removed, with a successful result. Another was seized with acute lobar pneumonia (pneumococcal) but made a good recovery, while a third contracted a whitlow a few days following his operation, but this did not in any way affect his recovery.

As regards the after-history of my patients, I can only say that I have seen them at periods varying from seven years to a few weeks after

their operation, and, except in a very few instances, they have been quite satisfied and have told me that the joint was as strong as ever. In part proof of this I would refer you to the cases in which after the semilunar cartilage in one knee has been removed, the patients have returned to have a torn cartilage removed from the other, or in one or two cases the other cartilage of the same knee. They would not have done this if the first operation had not been successful. Again, where I have operated in the case of both amateur and professional football players they have all played again, and many of them are still playing. One Monday morning, a week or two ago, I noticed in the column of the *Daily Telegraph* devoted to the account of Association matches played the previous Saturday, that a player in an important Second League match, from whose left knee I removed both semilunar cartilages at the same operation on March 16, 1910, had not only played well, but scored the only goal of the match.

Where a man is engaged in manual labour, I allow him to return to work in ten or twelve weeks after the operation, but in many cases—and this, of course, applies to sufferers who have sustained the accident at football (other than professional), and so are not entitled to workmen's compensation—they have returned to work as early as six or seven weeks after, and with no bad result.

I am afraid my remarks and conclusions have been, perhaps, based too much on personal experience, but inasmuch as so little has been authoritatively written about injuries to the semilunar cartilages in textbooks and elsewhere this was unavoidable. I trust my small contribution to the subject may be of some value, and would add, in conclusion, that I have always thought these accidents, which claim as their victims a goodly number of those engaged in the important industry of coal-mining, have not received the attention they deserved.

## LIST OF SPECIAL CASES.

|                 |   |
|-----------------|---|
| No. 49 ... ..   | Both internal cartilages removed at same operation        |
| Nos. 86 and 361 | " " 5½ years' interval                                    |
| " 123 and 146   | " " 9 months' "   |
| " 210 and 366   | " " 2 years' "  |
| " 374 and 449   | " " 9 months' "   |
| " 424 and 438   | " " 6 weeks' "  |
| " 62 and 70     | Both external cartilages removed at 1 year's "            |
| " 22 and 343    | Both cartilages in one knee removed at same operation     |
| " 113 and 266   | " " with interval of 3 years                              |
| " 184 and 195   | " " 8 months  |
| " 294 and 316   | " " 11 "  |
| " 110 and 142   | Same cartilage operated upon twice                        |
| No. 196 ... ..  | Patient developed gangrenous appendicitis after operation |
| " 428 ... ..    | " acute lobar pneumonia "                                 |
|                 | " whitlow "   |

## DISCUSSION.

Mr. MCADAM ECCLES said the Section had had two very interesting papers: that from Mr. Walton of a theoretical character, and the one from Mr. Martin exceedingly practical. Surgeons in London did not have the same opportunities of examining large numbers of accidents to the knee cartilages as did surgeons in the North; hence he hesitated about venturing an opinion as to their causation. But he thought that what Mr. Martin had said, particularly in connexion with coal-miners, tended to bear out the old-established idea that it was a twist of a flexed joint which was usually the cause of the injury, and that it was in strong, muscular men that the accident occurred. He noted particularly that it was the working of the coal while the miner was in a stooping posture, and he had seen one or two cases in which the same action caused the trouble in a non-miner. In one case the man was digging, and the accident occurred when, on stooping, he threw up a heavy spadeful of earth. With regard to the lesion occurring from movement on rough and uneven ground, it was, as a rule, when the joint was bent by the foot being put forward, and the body-weight coming more on to the internal than on to the external condyle, with the foot a little everted, and then a rotation of the femur occurred on to the head of the tibia. The fact that the foot was fixed and the femur twisted had not, he thought, been sufficiently emphasized. With regard to the sex preponderance, at St. Bartholomew's Hospital during the eight years 1902-09 inclusive there were 149 operations for displaced or torn semilunar cartilages, and of these 126 were in males. With regard to the anatomical condition, inspection of all specimens showed clearly that the internal cartilage was far more firmly fixed in its circumference, but far less firmly fixed so far as its antero-posterior extremities were concerned. The anterior cornu was exceedingly thin and narrow, and it passed forward into the transverse ligament to a large extent, but a little into the tibia. The posterior end he did not think was quite proportionately drawn in the diagram exhibited. There was practically very little sway of the cartilage inwards and outwards from the centre of the joint. He agreed that it was not common to find true tearing away of the anterior cornu of the internal semilunar cartilage, but there was more often a splitting longitudinally. Neither of the authors had quite explained why that splitting occurred. With regard to diagnosis and treatment, he thought it might be said that all surgeons considered that most cases of so-called internal derangement of the knee-joint were associated with some injury to the internal semilunar cartilage. An important point which had been raised was as to whether one ever found healing and practically complete restoration of the joint function without operative interference. In other words, was it worth while, in these cases where there was a definite history of damage to an internal semilunar cartilage, to endeavour to allow Nature to bring about a good result? He thought it was. Personally, he would be willing to have his joint placed in plaster of Paris for four weeks, with a good



layer of cotton-wool to continue sufficient pressure when the effusion was absorbed; and at the end of that time he would have a carefully carried out course of massage, not only—as was often done—to the joint itself, but also to the muscles which move the joint. But he was sure that if there was the least remnant of disability, or any recurrence of the condition, the sooner the joint was operated upon the better, because one saw—more often ten years ago than recently—cases where there had been many recurrences, and as a result the joint was disorganized. In his view it did not matter whether the incision was vertical, horizontal, or oblique, so long as the internal lateral ligament was not damaged. If one did accidentally divide fibres of the internal lateral ligament it was most important to suture them very carefully. He had not seen a case where the joint was badly damaged by operation. The only case of damage to the external cartilage he had dealt with occurred in a boy at the age of 7, in whom this cartilage was completely torn away in its circumference, but it remained attached at its antero-posterior cornu, and had slipped into the inter-condylar space.

Mr. JAMES BERRY said that when he was in Newcastle a year or two ago he had seen Mr. Martin operating through a transverse skin incision along the upper border of the cartilage, and he was so much impressed by the advantage it possessed over the vertical incision that he had changed what had been his practice of many years, and in all the cases he had operated upon since had employed the transverse incision, and had been well satisfied with it. He believed that surgeons did not make sufficient use of that very useful method of opening the knee-joint for this injury. Another point which Mr. Martin did not allude to, but which was important if others were to obtain results as good as Mr. Martin's, was the extreme celerity with which Mr. Martin operated. He would like to know what was the average number of minutes which that gentleman took to do the operation. He had seen him do four in less than an hour, and that was in favourable and marked contrast to the time taken by some surgeons.

Mr. ECCLES, in view of Mr. Berry's remark, desired to explain that he never used the vertical incision, but always a curved incision, extending along the anterior edge of the internal ligament, and then horizontally forwards between the two bones. This gave a flap which one could turn up, and it gave even more room than did the horizontal incision.

The PRESIDENT (Mr. G. H. Makins, C.B.), in calling upon the authors for their replies, said it would be interesting to hear an argument as to the mode of production of the injury, whether by forced extension, or whether it occurred during the position of flexion. It seemed to him that Mr. Walton, who appeared to have paid a great deal of attention to the subject, made out a very good case for consideration in favour of the mechanism being a crushing of the anterior part of the internal semilunar cartilage, though he had not, himself, thought of it from that point of view before. It seemed a good explanation of the longitudinal fractures at the anterior part of the internal semilunar



cartilage. His own experience was only that of a surgeon in a general-hospital, but most of the fractures in this position which he had met with had been transverse ones. The incision recommended by Mr. Robert Jones with the knee in the flexed position he had felt a great advantage, and it was more convenient than the position adopted before.

Mr. WALTON, in reply, said that until he received an abstract of Mr. Martin's paper he had not realized how common the condition under discussion was in miners. Although he felt sure that a satisfactory explanation existed, it was difficult to find one at so short a notice. He had come across one or two men who had worked as miners, and on questioning them he found that they were in the stooping posture, but as they threw the coal they rose from the stooping position, and it was then that the accident happened. They had stretched and slackened their ligaments through perpetually stooping, and the cause of the displacement was a forcible extension. He asked whether one could not consider that the injury resulted while the man was raising himself from the stooping position; and, answering the remark of Mr. Eccles, he did not know how a man could throw up a heavy spade of earth without raising himself to the upright posture. With regard to the "locking," this was the type of condition which he had gone into. Mr. Martin said that in these cases there was locking of the joint, and then recovery. This, of course, was true, but it did not throw light upon the cause, for if the primary lesion was caused when the leg was in the extended position and hyper-extension caused the injury, then the cartilage, being injured, passed during flexion between the two bones and prevented their approximation—i.e., prevented extension of the leg; so it did not enter into the question as to what was the primary cause. He laid stress on whether there was injury of the internal lateral ligament, because it appeared to him that if this condition was brought about while the leg was in a position of semiflexion and was caused by external rotation and abduction, one was bound to have a lesion frequently of the internal lateral ligament, and Mr. Martin stated that not uncommonly he found such a lesion, and yet he said that in the treatment of these cases one must take care not to injure the internal lateral ligament. It seemed difficult to reconcile these two statements. He had not found anything like rupture of the internal lateral ligament. Mr. Eccles said one must believe that the condition was produced when the leg was in semiflexion; but could Mr. Eccles reproduce the tendency in any knee-joint in a condition of semiflexion? He (Mr. Walton) had failed in his efforts to do so. With regard to the diagram which Mr. Eccles criticized, he admitted that it was somewhat exaggerated in order to emphasize the point he was making. Still, he had represented there only the cartilage itself; he had not put in the anterior or posterior horns, and if one omitted the posterior horn, then the posterior part of the cartilage would be found to be nearly as wide, relatively, as he had represented it. With regard to the explanation of the longitudinal tear, he thought he had made that clear. He thought the longitudinal tear might occur as a primary or as a secondary

lesion; it was due to compression between the anterior and posterior ends of the tibia. With regard to the incision, he had only twice tried the incision recommended by Mr. Barker, and it struck him as being valuable. Mr. Barker laid stress on the fact that in the early stages a longitudinal tear might start on the under surface, so that if one made the ordinary approach one was in danger of overlooking this injury. Mr. Barker's method of cutting down on the head of the tibia below, and then reflecting up the periosteum, capsule and cartilage, and so revealing the under surface of the cartilage, was very valuable from this point of view, and he was very pleased with the perfect view which it gave of the cartilage and the joint.

Mr. MARTIN, in reply, said he did not think it likely that Mr. Walton had ever been down a coal-mine, at least one in Northumberland or Durham; otherwise he would know that the miner generally had to work in such positions that it was impossible for him to assume more than the semi-upright posture while hewing the coal. Therefore, he felt that in the coal-miner the resumption of the upright position while bearing the strain had nothing to do with the causation. He agreed with Mr. Eccles as to the foot being fixed when the accident occurred, and he thought he had made this plain when speaking of the studs in the footballer's boots tending to fix the foot while the forcible motion of the leg was being carried out—particularly swerving. With regard to the splitting of the cartilage, he had always thought that the part of the cartilage near the free edge became fixed or nipped between the condyle and the tuberosity, that it was then dragged towards the centre of the joint. The amount of dragging was limited and a tear resulted, in the same way as in paper when pulled on from opposite directions. He did not operate in the case of primary tear unless there was permanent inability to extend the joint. Such cases he treated by prolonged rest, followed by massage. But in the event of subsequent attacks he did not hesitate to recommend operation.

## **Surgical Section.**

November 12, 1912.

MR. G. H. MAKINS, C.B., President of the Section, in the Chair.

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### **A Discussion on Sarcomata and Myelomata of the Long Bones.**

Opened by Sir ALFRED PEARCE GOULD, K.C.V.O., M.S.;  
Sir JOHN BLAND-SUTTON, F.R.C.S.; Sir FREDERIC EVE,  
F.R.C.S.; G. E. GASK, F.R.C.S.; and ARCHIBALD D. REID.

#### **OPENING ADDRESS WITH REGARD TO CLINICAL DIAGNOSIS.**

SIR ALFRED PEARCE GOULD, K.C.V.O.: I have been asked to make a few remarks upon the diagnosis of sarcoma of long bones. The only recent addition of first-rate importance to our clinical methods of establishing the nature of a swelling on or about a bone is the information we receive from a good skiagram. It would be improper for me to enter upon this important part of the subject, as I see that it has been specially allocated to Mr. Reid, who is to follow me later on. I am, therefore, limited to dealing with the diagnosis of sarcoma of long bones by our older methods of examination. I do not propose to discuss these in any full or systematic manner, as you are all so familiar with them, but I shall limit myself to indicating what seem to me to be the most important clinical features of sarcoma and myeloma of long bones, and to mentioning two or three conditions which I have known give rise to some difficulty of diagnosis.

The stage of the disease in which there is no palpable swelling, merely slight pain in the bone of an aching or boring character,

generally made worse by use of the part, presents nothing to our ordinary methods of examination by which we can arrive at a diagnosis, and the aid often rendered by X-rays at such a time is simply invaluable.

The case that is more usually presented to us is that of a swelling of a bone, recently noticed, steadily enlarging, and attended with gradually increasing interference with the function of the part. The swelling of a sarcoma is usually a single swelling, it may project on more than one aspect of the bone, but it is continuous between these prominences, and they can be recognized as two or more bulgings of one and the same tumour. It is always, of course, absolutely fixed to the bone, and in the early stages it presents very slight, if any, nodulation of the surface.

A periosteal sarcoma exhibits a marked tendency to extend rapidly along and around the diaphysis, and to ensheath the bone. Later on it penetrates and replaces the bone, and leads to spontaneous fracture, and also invades the neighbouring muscles. Its surface, then, may be even or coarsely lobed; in consistence it is firm, especially when it has undergone chondrification or ossification. When such a tumour has developed all these features, and especially when its very rapid growth, and the occurrence of secondary growths in glands or lungs have shown its great malignancy, the diagnosis can present no difficulties. These arise when the growth is small, or departs in some striking way from the usual course. In a very small periosteal sarcoma the important features to recognize are its absolute fixity to the bone, its well-defined outline—for it stands up on the surface of the bone, and does not gradually shelve off like an inflammatory swelling—and the absence of lobulation of the surface.

The earliest periosteal sarcoma that I remember to have seen was the case of a young man, aged 18, brought to me last May by Dr. Bergin, of Bristol. There was a history of tripping on the stairs nine weeks before I saw him, and again three weeks later; then a slight limp developed, and Dr. Bergin found a firm lump in the thigh which he hoped was a hæmatoma. With rest and counter-irritation it seemed at first to improve, but then the lump was found to be enlarging, and to be the seat of pain on quite trifling jars. I found a small elongated swelling on the anterior surface of the lower part of the shaft of the right femur, but small as it was its edge was abrupt, and stood well above the surface of the shaft of the bone. Had it been an inflammatory swelling, the edge would have been ill-defined and

shelving. X-rays assisted us only so far as they showed the bone to be intact, and the lump to be a deposit of some kind on the surface of the bone. The patient refused to submit to amputation, and I therefore advised him to have radium inserted into the tumour. This gave me the opportunity of removing a portion of the growth for microscopical examination and of verifying the diagnosis. I may just say, in passing, that there is reason to believe that the use of radium has arrested this growth, and I hope it has cured the lad.

A para-osteal lipoma may be very difficult to distinguish from a sarcoma if there is no accurate history. Although growing from the periosteum it is not so immovably fixed to the bone as is the sarcoma, its surface is finely lobulated, and its consistence is less firm than that of sarcoma. Covered over with a thick mass of elastic muscle, however, it is very difficult to recognize with certainty these features, and when the tumour has been only quite recently noticed, although really congenital in origin, the diagnosis may be so difficult as only to be established by an exploratory incision.

Another difficulty is that presented by a periosteal sarcoma growing out from the bone as a globular tumour, without showing any tendency to invade the periosteum extensively. Occurring at or near the end of a diaphysis, such a tumour resembles a chondroma or exostosis. I remember seeing a sarcoma of this kind on the inner side of a young woman's thigh; it was about the size of an orange. Here, again, an accurate history, if obtainable, will be of the utmost value; in its absence we have to depend upon such signs as the more even outline and the pain of the sarcoma, the extreme hardness and more pedunculated attachment of the exostosis, and its painlessness.

The difficulty is greater where the benign tumour acquires a broad and extensive attachment to the bone, for it then resembles a sarcoma much more closely. I have seen two such cases where difference of opinion was expressed; one of them was in a girl with a tumour of the upper end of the humerus; a surgeon had just seen her and had advised immediate amputation of the entire limb, as he regarded the growth as a sarcoma. I found a large tumour of the upper end of the bone, very firm, with a sharply defined outline, but very nodular; it was attached to the bone immediately below the head, and did not extend down along the shaft. A skiagram showed an uneven growth of bone around the humerus. The extremely nodular character of the tumour, its very abrupt outline, and the absence of any tendency to grow down along the shaft, led me to advise that this was not a sarcoma but

an osteoma, and that as it did not interfere with the movements of the shoulder-joint it might be left alone. I saw the patient a few years later; no further growth had occurred. Two years ago a man, aged 32, was under my care at Middlesex Hospital with a large tumour of the upper end of the right humerus. In this case, again, the tumour was very uneven; it was attached to the bone all round the upper end of the shaft, except for a finger's breadth on the inner side. Roughly it corresponded in extent to the surface beneath the deltoid muscle, but it projected both behind and in front of that muscle. It was entirely sessile, with a sharply defined outline, and, as I have said, had a very nodular surface. The man stated he had known of a lump in this situation for eight years, and that during the last few months it had rapidly enlarged, and it was now interfering with the movement of the arm. The skiagram showed that the humerus was not invaded with the tumour, which was a broadly attached, very nodular growth. In spite of the suspicious history and appearance, the extremely nodular surface of the tumour led me to decide that this was not a sarcoma but a chondroma, and to advise removal of the tumour and not amputation. I saw the man last July; there was then no sign of recurrence of the growth. The pathologist reported that the tumour was a simple chondroma, calcified in places.

The difficulties associated with the diagnosis of central sarcoma and myeloma are more frequent and are primarily due to the fact that we are unable to feel within the bone and to appreciate some of the essential features of the growth. Speaking generally, the diagnosis rests upon recognizing a disease which replaces the cancellous tissue of an epiphysis, then expands the thin shell of bone, and finally penetrates this and luxuriates in the tissue outside the bone. In its growth it exhibits a marked tendency to assume a more or less globular, or at least ovoid, outline, and does not as a rule invade a great length of the bone. This is a striking feature when contrasted with what is seen in periosteal sarcoma. The central sarcoma as distinguished from the myeloma shows more tendency to destroy bone; it expands the bone less, it penetrates it quicker, it luxuriates around it more rapidly—in other words, it is a more active and more malignant growth. Then, too, it occurs at other situations than the epiphyses, and will rapidly cause spontaneous fracture of the shaft of a bone. Myeloma is less rapid in its growth, is long shut up within the expanded bone or tense periosteum; and it does not penetrate the articular cartilage and invade the neighbouring joint.

True expansion of the bone is a sign of the greatest importance, and the more limited the area of bone expanded, and the greater the degree of expansion, the more characteristic this sign, and the more likely is the tumour to be a myeloma rather than a sarcoma. The absence of new bone laid down on the surface of the enlarging bone is a striking distinction between a sarcomatous growth and a tuberculous, syphilitic, or inflammatory ostitis.

I have already pointed out that in the case of a central sarcoma in the earliest stage only the X-ray can demonstrate its presence. But the increasing growth of a sarcoma is attended with other features that enable us to identify it. In a myeloma particularly we notice the globular outline of the tumour and its expansion of the bone into a similar globular form. In no other disease is the globular expansion of an epiphysis carried to such a degree; the swelling shows no tendency to extend along the shaft, and to involve more and more of the length of the bone. The cancellous bone is rapidly destroyed, and the outer shell of bone is truly expanded; there is no real thickening of the bone from new deposit on its outer surface. This is a striking contrast to the condition found in tuberculous or coccal infection of an epiphysis. The yielding of the thin shell of bone under the compressing finger, giving the sensation of "egg-shell crackling," is occasionally felt; it can only be detected during one phase of the growth; the buckling in of the tensely stretched periosteum, when the outer shell of bone has been destroyed, is just as characteristic if the surgeon is fortunate enough to recognize it. Along with this expansion of the bone there is a similar change in the articular cartilage—it becomes flattened out over the growth, but its integrity is preserved long after that of the bone is lost, owing, no doubt, to its avascularity and to the extreme slowness of all nutritive changes in cartilage. There is the same absence of irritative change that there is in bone; adhesions do not form in the joint, and smooth movement of one bone over the other is preserved, its range being limited only by the disproportionate size of the articular surfaces.

As an illustration of a difficulty in diagnosis, I would mention a case of osteomyelitis fibrocystica sent to me at Middlesex Hospital five years ago with a diagnosis of sarcoma of the humerus made by a surgeon and confirmed by a radiographer. The patient was a boy, aged 13. I found an enlargement of the upper part of the diaphysis of the right humerus extending into the epiphysis, the bone formed an elongated swelling, and the skiagram revealed a considerable



enlargement of the medullary cavity, with great thinning of the bone. I decided that this was not a sarcoma because of the tubular form of the dilatation of the bone—the absence of all globular growth. On cutting into the bone, I found the medullary cavity greatly enlarged and filled with pink serous fluid. I could not scrape away any cyst wall or trace of growth. The cavity gradually filled up, and the boy left the hospital with a sound arm.

Two features sometimes met with in sarcoma of bone call for special mention—they are pulsation and fluctuation. If pulsation is detected in a tumour of bone, it is, I believe, diagnostic of a myeloma or of a central sarcoma. In some cases the pulsation is very obvious, but in others it requires great care in the examination to detect it. The pulsation, felt when an artery is raised over a tumour beneath it is felt only along the line of the vessel, and often the contour of the artery can be recognized. The pulsation of an aneurysm is usually much more forcible than that in a sarcoma, and when it is arrested by compression of the artery above the aneurysm shrinks, or can be compressed by the hand, and is felt to become more tense and to fill out again when the compression of the artery is removed. A pulsating sarcoma merely ceases to pulsate when the main artery of the limb is controlled, and no change in its size or tension occurs. In most cases the pulsating sarcoma occurs in a situation where an aneurysm cannot arise, and the associated expansion of the bone affords a further ready means of distinction.

The extreme softness of some sarcomata may make them give the sensation of true fluctuation, and more often they are so elastic that it is difficult to distinguish them from fluid swellings; they are then liable to be mistaken for an abscess or a cyst. The absence of inflammatory phenomena, the expansion of the bone without any sclerosis or new deposit on the surface, and in some cases the presence of firmer and non-fluctuating portions of the swelling, are the points upon which one relies for diagnosis from abscess. A cyst is more tense than a very soft sarcoma.

Hydatid of a long bone is very rarely met with in this country; I have never seen a case. I mention it now only to remind you that its accompanying eosinophilia is a valuable addition to our means of distinguishing it from sarcoma.

## OPENING ADDRESS WITH REGARD TO PATHOLOGY.

SIR JOHN BLAND-SUTTON: No one will deny that the phrase "sarcoma of bone" is conventionally applied to all varieties of primary malignant tumours of bones. It includes sarcomas which arise spontaneously, as well as the excessively malignant tumour which sometimes follows a single intensive injury. There are tumours of bones concerning which, after a microscopic examination, an opinion can be definitely expressed for or against malignancy, and there are others in which the most expert histologist, aided by every kind of differential staining reagent, hesitates to call innocent or malignant. A spindle-celled peripheral sarcoma of the femur in a youth leads the surgeon to amputate the limb at the hip-joint. The patient recovers easily and speedily from the operation, but dies of recurrence, or from secondary deposits in the lungs a few months afterwards. A sarcoma with the same microscopic characters grows from the tibia of a child; the leg is promptly amputated at the knee, and seven years later the child is alive and well. Years ago I thought that sarcomas in the proximal were more rapidly fatal than those in the distal bones of the limbs. I do not think so since I have seen death induced as rapidly by a sarcoma of a metatarsal bone as by one in the femur. The size of a bone counts for little; a sarcoma of the clavicle is as deadly as one arising in the ilium. On clinical grounds surgeons can differentiate between typical chondromas of the metacarpal bones and chondrifying sarcomas of the tibia or scapula, but they are puzzled when a man with several apparently innocent chondromas which have lodged in his bones quietly for many years, complains that one is growing quickly, and within a few months he dies with secondary cartilaginous nodules in his lungs. All who have studied histologically the exuberant material of repair around the seat of fracture in a long bone know the difficulty of deciding whether the new tissue is malignant or innocent. Such difficulties have induced surgeons to mock at the efforts of morbid anatomists, but histology helps, not only in the classification, but also in the diagnosis and prognosis of sarcomas of bone. No one will deny that the separation of myeloid tumours from sarcomas has been justified by experience, and many useful limbs have been saved in consequence. As I have devoted much study to myelomas, my remarks will be mainly occupied with this genus and certain tumours which counterfeit them.

Myelomas grow chiefly in the shafts of long bones immediately adjacent to the epiphyseal line. I have never seen one which arose in an epiphysis. A myeloma in the upper end of the radius of a youth often has the discoid epiphysis of the head of the bone resting on the crown of the tumour, resembling a lid on a jar (fig. 1). Myelomas

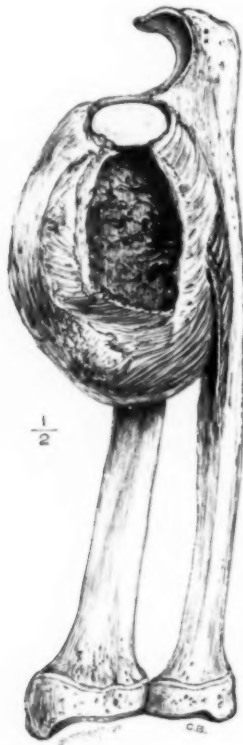


FIG. 1.

A radius and ulna. The neck of the radius is expanded by a myeloma. The epiphysis is unaffected.

arise during childhood and adolescence, and they are more frequent in the long bones of the lower than in those of the upper limb.

The clinical and pathological features of myelomas are well known: these tumours grow slowly and cause expansion of the surrounding bone; they are extremely vascular and in colour dull red or maroon. Histolo-

gically they resemble the red marrow of bone and contain multinuclear cells in abundance. Extravasations of blood are common in the tissues of such tumours and degenerative changes lead to the formation of cysts in them.

Since myelomas have been separated from the disreputable society of sarcomas, an endosteal tumour other than a myeloma, uniformly expanding the bone in the shape of the familiar spina ventosa, is a rare occurrence.

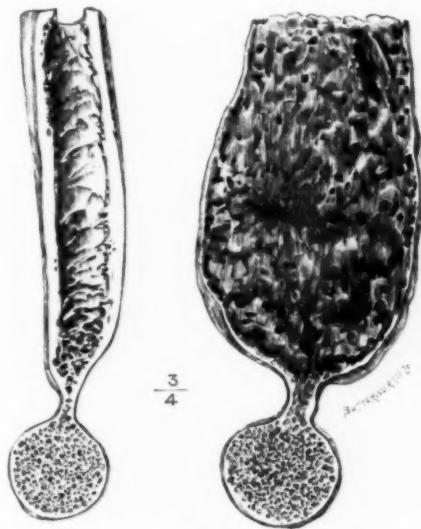


FIG. 2.

The lower end of a humerus in longitudinal section: it contains a central tumour with the microscopic structure of a perithelioma. The figure on the left shows the corresponding section of a normal humerus.

The naked-eye characters of myelomas are so striking that surgeons sometimes fail to make a thorough examination of central tumours of bone. There are endosteal tumours which resemble myelomas in colour, consistence and vascularity, as well as in clinical conduct, but differ from them in structure. Myelomas are so essentially tumours of childhood and adolescence that a red endosteal tumour, occurring in an unusual situation at an unusual age, should be critically investigated. For example: A medical man injured his arm whilst dancing on board ship. During the dance, which began as "drawing-room lancers" and

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ended as "kitchen lancers," the patient felt pain in his arm whilst swinging around a stout partner. A year later I found the lower fourth of the humerus enlarged, and a skiagram showed considerable uniform expansion of this part of the shaft, but there was no "egg-shell crackling." The clinical signs were those of a myeloma, but as such a tumour is rare about middle life, I obtained a piece of it for microscopic examination: the interference caused the tumour to bleed as freely as if a cavernous nævus had been incised. The microscopic characters were remarkable, and induced me to excise the lower fourth of the humerus instead of removing the limb at the shoulder-joint (fig. 2). In naked-eye

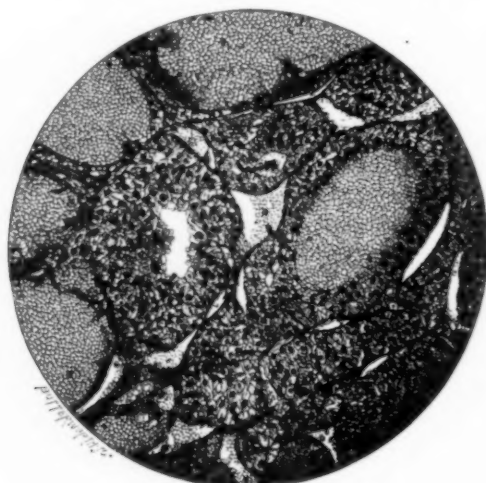


FIG. 3.

Microscopic characters of the red endosteal tumour of the humerus represented in fig. 2. ( $\times 1,000$ .)

characters this tumour is like a myeloma, but on microscopic examination no giant cells are visible, and its histological features resemble those presented by an endothelioma arising in a nævus. In the main the tumour has the structure of a cavernous nævus, and the blood-vessels, in some parts of the tumour, abut on each other, and in others they are separated by richly cellular tissue: some of the vessels are surrounded by the cell-mantle which is such a striking feature of the rare tumour described by Ziegler as an angio-sarcoma, now commonly known as a perithelioma. This peculiarity depends on an overgrowth of the cells in the perivascular sheaths of small blood-vessels (fig. 3).

A study of myelomas and endosteal peritheliomas throws, I venture to think, some light on another endosteal condition which has puzzled me very much, not only from the pathological standpoint but also clinically—I refer to what are known as benign cysts of bones, excluding cysts due to softening in cartilaginous tumours, cavities due to abscesses, and ecchinococcus disease. The following is a good example: A boy, aged 19, hurt his shoulder whilst leaving a motor-bus in motion. A skiagraph furnished evidence that the humerus was fractured at the surgical neck, but the bone at the seat of the injury



FIG. 4.

The upper fourth of a humerus split longitudinally. There is a fracture at the surgical neck. The shaft of the bone immediately below the epiphyseal line is hollow. ? Benign cyst of bone. Excised from a lad aged 19.

exhibited a shadow which suggested the presence of an endosteal sarcoma. After much careful consideration I excised the upper third of the humerus. When the exsected piece of bone was split longitudinally, the cancellous tissue of the bone immediately below the epiphysis was found hollowed out and the irregular cavity filled with pink fluid (fig. 4). The recesses in the osseous boundaries of the cavity contained fibrous tissue and large multinuclear cells.

I believe that some benign cysts of bones are closely related to myelomas; it is valuable evidence in relation to this matter that they commonly occur in the long bones of children and adolescents, especially in those bones and parts of the bones most frequented by myelomas, such as the lower end of the shaft of the radius, the upper end of the fibular shaft, and especially the upper end of the humerus. The epiphyseal cartilages, as with myelomas, act like neutral lines.

A myeloma is often the seat of bleeding, and the blood extravasated into the tissue of the tumour hollows out the centre and converts the tumour into what our immediate surgical predecessors called a malignant blood cyst of bone. The age-incidence, the distribution of benign cysts among the bone and the locality in special bones favoured by myelomas are identical. I have come to the conclusion that some benign cysts in the long bones of children and adolescents represent myelomas which have undergone spontaneous cure. The atrophy of the cell elements of a myeloma accords with the natural history of red marrow, for this tissue, relatively abundant throughout the shafts of bones during infancy and childhood, is gradually replaced by fat as the skeleton matures.

All benign cysts of bone do not arise from the retrogression of myelomas, some may arise from degenerative changes in peritheliomas, and I think that some endosteal peritheliomas, especially the specimen I have exhibited to-night, are cavernous angiomas of bone. Such tumours occur in every vascular organ, skin, mucous membrane, muscle, brain, liver, rectum and bladder. Cavernous angiomas in adolescence and early adult life are liable to many changes, some increase rapidly, others become peritheliomas, or regress and become cystic, and a few spontaneously disappear. The cancellous tissue of bone is very vascular, and as all vascular tissues may be the seat of cavernous angiomas, why not bone? I think that among the central pulsating tumours of bone formerly called osteo-aneurysms, some were myelomas, and some cavernous angiomas, or peritheliomas, and the latter tumours, like myelomas, sometimes undergo spontaneous cure and become benign cysts of bone. These are statements difficult of proof, but it is true that when asked to interpret skiagrams of a bone suspected to be enlarged by a sarcoma, we are at present unable to differentiate with certainty between the shadow cast by an endosteal sarcoma or an endosteal cyst. We still rely on pathology for diagnosis and prognosis, as well as guidance in treatment.



## INTRODUCTORY ADDRESS WITH REGARD TO TREATMENT.

Sir FREDERIC EVE : My remarks on the treatment of sarcoma of the long bones must necessarily, owing to the short time at my disposal, be mainly concerned with general principles. The sarcomata fall, for purposes of treatment, into three groups :—

(I) Periosteal sarcomata.

(II) Central sarcomata composed of round and spindle cells.

(III) Myeloma (myeloid sarcoma).

The last named must be differentiated from the diffuse or generalized hyperplasias of medullary tissue met with in albumosuria and other affections, and to which the term "myeloma" is also applied.

## (I) PERIOSTEAL SARCOMA.

The periosteal sarcomata spread locally along the periosteum, endosteally through the medulla, and also along the muscles attached to the affected bone. Extension into veins is so early that in many cases, especially of sarcoma of the femur and humerus, metastases are already present when the patient first comes under observation. Sarcomata of these bones frequently involve the axillary and femoral glands respectively.

Amputations in periosteal sarcoma must remove the affected bone in its entirety, and if possible the whole or a considerable part of the length of any muscles attached in the neighbourhood of the tumour.

Owing to the rapid growth of sarcomata of the humerus, the fact that they usually originate in the upper third, and their tendency, wherever arising, to involve the whole length of the bone, the interscapulo-thoracic (Berger's) operation will be required, except in the rare instances in which there is a growth confined to the lower third, when amputation at the shoulder-joint may suffice. Butlin<sup>1</sup> states that "there is no tendency to affection of the axillary glands," but the truth of this I doubt.

Notwithstanding arguments in favour of non-intervention based on the failure of treatment, I think that a patient with periosteal sarcoma of the femur should be given the remote chance afforded by amputation at the hip-joint. The immediate danger of the operation is slight.

<sup>1</sup> A writer in "American Practice of Surgery" expresses an opposite view.

I have performed, since 1896, eleven consecutive amputations at the hip-joint without a death. We can only hope that in the future the practitioner who first sees the patient, assisted as he is by the X-rays in diagnosis, will send patients for surgical treatment immediately, and that our statistics may thereby be improved. The femoral lymphatic glands are often palpably enlarged, and I have for many years been in the habit of removing them in the preliminary stage of the operation. The anterior racket incision has been used, the artery and vein being tied, and the glands dissected out through the first incision. In tumours situated high up in the femur I have dissected the attachments of the muscles cleanly from the os innominatum. The practice of a preliminary ligature of the main vessels, the injection of cocaine into the nerve-trunks before division, and other methods of combating shock, have greatly diminished the immediate mortality in high amputations at the shoulder and hip. I have frequently injected saline and brandy directly into the femoral vein before closing the wound.

The common periosteal sarcomata of the upper third of the tibia and those of the upper third of the fibula, together with rare tumours of the same nature in the forearm (usually in the upper third), should be treated by amputation at the lower third of the thigh and humerus respectively. In tumours of the lower third of the leg amputation through the knee-joint may be done. Considerable enlargement of the femoral glands in growths of the middle and upper third of the tibia has been noted by me. These have been removed, and although the pathologists reported that the enlargement was not due to malignant disease, I must own that I received this information with scepticism.

Sarcomata of the ribs are rare. They may now be dealt with safely owing to the recent methods of opening the pleura.

In regard to microscopic structure, after admitting that the round-celled sarcomata are the most malignant, I agree with Butlin that the metaplasia of part or the bulk of the tumour into cartilage or bone does not affect its malignancy, and therefore does not modify the treatment.

#### (II) CENTRAL SARCOMATA COMPOSED OF ROUND, SPINDLE, OR MIXED CELLS.

We owe our knowledge of the lower degree of malignancy of central tumours, together with much more in the natural history of malignant disease of the bones, to the painstaking work of Butlin. Their relative benignity must be ascribed to their being surrounded by a capsule

of bone, but we must not overlook the fact that in many instances there is a wide infiltration of the medulla; and in some the bony capsule has been broken through. When this has occurred they should, I think, be treated on the same lines as periosteal sarcomata. Otherwise it would appear safe to amputate through the affected bone some distance above the disease, if it occupies the distal end; or through the joint immediately above, if it occupies the proximal end of the bone. Central tumours of the lower end of the radius and ulna are less malignant than those of other bones. Butlin quotes ("The Operative Surgery of Malignant Disease," p. 52) a case of spindle-celled sarcoma of the lower half of the ulna which was treated by erosion and the patient was well two years later; and again (*op. cit.*, p. 52) a case of spindle-celled sarcoma of the external condyle of the femur treated by resection. The patient was in good health three years later. A central spindle-celled sarcoma of the upper end of the tibia was treated by Mr. Openshaw at the London Hospital by erosion and the patient was alive and well over six years after. Mr. Shattock and myself examined the microscopic sections. On the other hand, in an example of central sarcoma of the upper epiphysis of the femur, the patient died of the operation and was found to be already suffering from metastases (*op. cit.*, p. 51).

The tumours under consideration are rare, and therefore the experience of individual surgeons is very limited. If we are to learn more of the later histories of patients it must be by a combined system of registration at the various hospitals by which the patients are followed up.

I offer the above remarks on the treatment of this group in a tentative manner, and hope to learn the opinion of other surgeons. These growths, if well localized, and especially if spindle-celled, offer a tempting field for resection and the employment of the various methods of osteoplasty to be alluded to later.

### (III) MYELOMA (MYELOID SARCOMA).

Although it has long been taught that the true myeloma has a low degree of malignancy, yet it is only in recent years that it has been recognized as possessing, at least in some situations, a purely local malignancy. Butlin, even in 1900, classes the central round and spindle-celled sarcoma with the myelomata under the common heading of central tumours, in discussing their treatment. The broad general statement made in some text-books that the myelomata are

only locally malignant requires, however, considerable modification. The myelomata of the femur, and especially those of the upper end of the humerus, are sometimes followed by metastasis. According to Butlin's statistics, the tumours were giant-celled sarcomata in three out of five patients who died with metastasis after amputation of the femur for central sarcoma (op. cit., p. 53). And in two out of three unsuccessful cases of sarcoma of the upper end of the humerus two were described as myeloid sarcoma. Both died of metastasis after the performance of Berger's operation. Kausch (op. cit., p. 694) describes a case of myeloid sarcoma of the upper end of the humerus, treated in 1902 by resection and implantation of two sterilized portions of humerus. Recurrence necessitated amputation at the shoulder-joint. Death took place from metastasis eleven months after the first operation.

Our London Hospital statistics throw little light on this question as all the cases involving the femur and humerus were treated by amputation. They, however, emphasize the benignity of myeloma of the tibia and fibula. Mr. L. J. Austin has only been able to trace for me seven cases during the ten years 1902-11, inclusive. The cases were as follows: Myeloma of upper end of humerus (amputation at shoulder-joint), well after three years; of lower end of femur (amputation at hip-joint), well after eight years; of lower end of femur (amputation at middle third of thigh), well after three years. Two cases of myeloma of the upper end of the tibia and two of the fibula were all treated by local removal; three by resection and one (tibia) by erosion. They were all well at periods varying from one and a half to eight years. I examined microscopic sections from all these cases but one (femur).

As far as I can judge, this difference in nature depends rather on the seat of the disease than on the structure of the tumour. The nearer the body the greater the malignancy would appear to be true of the myelomata as well as of the periosteal sarcomata. I have examined sections of all the myelomata treated at the London Hospital since 1902, and find a very fair uniformity in their structure. It must be admitted, however, that one example of myeloma of the head of the humerus looks very malignant. This patient was, however, well three years after amputation at the shoulder-joint. There are a large number of myeloplaxes lying among oat-shaped spindle and a few round cells; and I do not observe the tendency to fibrillation or the formation of fibrous tissue apparent in most myelomata. I suspect that the old statistics have been made less favourable by the inclusion among myelo-

mata of a certain number of round- and spindle-celled tumours containing a few multinucleated cells such as are present in many rapidly growing neoplasms.

In the long bones the myelomata are met with so frequently in four situations, that their occasional occurrence elsewhere is negligible in considering their treatment. These situations are the epiphyseal extremities of the upper ends of the tibia and fibula, the lower end of the femur, the lower end of the radius, and the upper end of the humerus. Their frequency (excepting the fibula) is in the order named: and it may be noted that these are the epiphyses which are the last to unite to the diaphyses. The treatment adopted must depend on the size and extent of the tumour and its locality. The following operations are employed: (1) erosion, (2) resection, (3) amputation.

(1) Erosion may be adopted in tumours of moderate size, when the bony walls are intact and sufficiently strong to bear pressure after the removal of the tumour. The cavity, if moderate in size, may best be filled with paraffin having a melting-point of about 110° F. This sets sufficiently hard at body temperature and is easier to manipulate than a paraffin with a higher melting-point. I have also used gelatine and iodoform successfully. Larger cavities may be filled with decalcified bone-chips, or better with chips taken from a recently amputated limb. There is very free hæmorrhage from the cavity, even if of quite moderate size, so that the use of an elastic tourniquet should not be neglected. The walls should be swabbed with pure carbolic or touched with Paquelin's cautery.

(2) Resection: This will usually be required in myelomata of the bones of the lower extremity where the osseous wall is so thinned that it would collapse or "concertina" after removal of the growth. It might also occasionally be resorted to in quite early growths of the upper end of the humerus. Myelomata of the lower end of the radius and the upper ends of the tibia and fibula (especially the radius) are by far the most favourable for treatment by erosion or resection.

(3) Amputation immediately above the tumour may be required when the disease has penetrated the bone and widely infiltrated the soft parts. It must be especially borne in mind that conservative treatment is much less likely to succeed in myeloma of the upper end of the humerus and in both ends of the femur, for the reasons given above.

The true myelomata can usually be recognized by their slower growth, distinct delimitation, the absence of infiltration of bone, their

maroon-red colour, and often the presence of pulsation at some point.

A surgeon about to operate for sarcoma, especially if it be a central tumour, should have a microscopist in attendance for the purpose of making a fresh section. The appearances of a myeloma are so characteristic that a fresh section will suffice, but in certain cases it may be advisable to postpone operation until a more careful microscopic examination of a portion of the tumour has been made. I am of opinion that the danger of infection of surrounding tissues by an exploratory incision has been much overrated. Even if a tumour turns out to be a very malignant one and implantation in the incision occurs, the affected area would undoubtedly be removed.

I may mention incidentally three cases of myeloma treated successfully by erosion or resection:—

In a man, aged 35, I removed with the surrounding tissues a myeloma of the upper end of the fibula which had freely burst through the capsule of bone. The microscope showed that the muscles were infiltrated with round cells and myeloid cells. He was quite well eight years and four months afterwards.

A man, aged 22, was treated for a myeloma of the head of the tibia by erosion. He was well five and a half years after.

A young married lady was treated for myeloma of the lower end of the radius by resection of the lower extremities of the radius and ulna and shortening of all the tendons of the wrist. She was well twelve years after, and could use her hand—the right—for writing, sewing, &c.

The recent advances in the surgery of transplantation of bone, cartilage, and even of joints, have opened up a new field for the treatment of myelomata in selected cases. A portion of bone from the same individual may be utilized (autoplasty) or from an amputated limb or a corpse (homoplasty).

In the first category the fibula has been widely used, especially in resections of the upper end of the tibia. After the removal of the diseased portion of tibia, the upper end of the fibula is driven into a hole made in the head of the tibia (if it has been left) or into the lower end of the femur. At a later operation the fibula is cut across lower down and driven into the distal end of the tibia.

I am able to show a young woman from whom I removed by resection of the upper third of the tibia a large myeloma which had spread widely among the surrounding structures. The femur and tibia were united by bolting them together with a portion of the patient's own fibula,



gap of nearly 2 in. being left between them and the limb thereby lengthened. The later skiagrams appear to show that there is a new formation of bone beneath the periosteum of the implanted fibula. It is now a year and seven months since the operation; there is no recurrence, and she can walk with a poroplastic support, but the union is not firm and the shortening amounts to  $4\frac{1}{2}$  in. I attempted to get greater solidity by separating a portion of the anterior margin of the tibia, carrying it across the gap, and pegging it into a groove in the femur. If I had the opportunity again I should graft in a portion of tibia covered with cartilage. Janeway took a fragment of tibia from the same individual to replace  $5\frac{1}{2}$  in. of ulna resected for sarcoma. A defect in the radius resulting from osteomyelitis has been successfully filled by separating a portion of ulna and twisting it on the interosseous membrane into the gap.

When autoplasmic grafts are used the periosteum of the graft should be preserved. It is stated that the periosteum lives, while the bone itself dies and is absorbed, but is gradually replaced by new bone formed by the periosteum of the graft and the medulla of the bone into which it is grafted (Lexer, Axhausen). The truth of this appears, however, to be controverted by an instance of transplantation of dead bone carried out by Kausch.<sup>1</sup> He removed the head of the tibia with its periosteum for myeloma and grafted 8 cm. of a tibia from an amputated limb. The graft was previously deprived of periosteum and medulla and treated with alcohol, ether, and boiling water. Amputation was performed for recurrence nine months later. A longitudinal section of the bone showed that the graft was necrotic and without apparent trace of organization, but was surrounded by a complete mantle of periosteum continuous with that of the pre-existing bone. Under the microscope could be followed the two processes of destruction and reconstruction, the newly formed periosteum penetrating cavities in the bone.

Küttner,<sup>2</sup> of Breslau, has published three remarkable cases of malignant tumours of the lower extremities in which bone and articular surfaces of corpses were used for grafts. Two cases were chondrosarcomata of the upper end of the femur. The upper third of the femora together with the heads of the bones were removed and the parts replaced by grafts of corresponding extent. Union of the graft to the grafted bone took place and the hip-joints were movable. The

<sup>1</sup> *Beitr. z. Klin. Chir.*, Tübingen, 1910, lxxviii, pp. 670-716.

<sup>2</sup> *Idem*, 1911, lxxv, pp. 1-38.



first patient died of metastasis thirteen months after the operation. In the second recurrence occurred, and a spontaneous fracture of the graft, which, however, united. In a third case described as a malignant chondroma (? chondro-sarcoma) involving the upper end of the tibia, the affected portion of bone with the articular surface was resected and replaced by a corresponding graft taken from a corpse. Healing took place with a fistula, but the knee-joint could be bent to an angle of  $45^{\circ}$  and the patient could stand and walk without an apparatus. In one case the subject from whom the graft was taken died as long as twenty-four hours before the operation. Ivory pegs were used to fix the graft to the grafted bone in the first case; and portions of fibula were employed to bolt the bones together in the other cases.

It is quite evident from the above brief summary that grafting has a future before it; but we need not fear that in this country enthusiasm for experimental surgery will lead us to perform such unjustifiable operations as resection of periosteal sarcoma of the femur.

I have been especially asked to make some remarks on the treatment of sarcoma with Coley's fluid. Coley advocates the use of this fluid, first, in cases of sarcoma of the long bones in which operation means a sacrifice of the limb. If no improvement is observed at the end of two or three weeks he advises operation. He writes that the greatest value of the toxins in sarcoma of the long bones would be shown to lie in a judicious combination with conservative operative treatment. In sarcomata of the myeloid type particularly, partial operations can be safely substituted for amputation. Secondly, he considers the use of the toxins as a prophylactic against recurrence as offering by far the most important field. Thirdly, he employs the fluid in cases of inoperable sarcoma. I have the pleasure of being personally acquainted with Dr. Coley, and was greatly impressed by his enthusiasm and candour. It is impossible to gainsay such statistics as the following ("Final Results of Cases of Sarcoma in various Situations"):<sup>1</sup> "Seven remained alive and well at the end of fifteen to eighteen years; seven remained alive and well at the end of ten to fifteen years; seventeen remained alive and well at the end of five to ten years; ten remained alive and well at the end of three to five years. That is, forty-one cases remained well from three to eighteen years, or thirty-one from five to seventeen years."

"As to the correctness of the diagnosis in these cases, they were

<sup>1</sup> *Surg. Gynec. and Obstetr.*, &c., Chicago, 1911, xiii, pp. 174-190.

practically selected cases—i.e., selected by the leading surgeons of America, as hopeless, inoperable cases. In all these cases, with the exception of four, the diagnosis was confirmed by careful microscopical examination in most cases not by one, but by several of the most competent pathologists." Yet it is astonishing that as far as I have been able to ascertain, anything at all comparable to these successes has not been met with elsewhere.

Mr. L. J. Austin, one of our surgical registrars, has been at much trouble in looking up the cases in which Coley's fluid has been given at the London Hospital. The treatment has been started in many cases, but has been discontinued for various reasons. All cases are excluded unless ten or more injections were given. They number only ten. In seven there was absolutely no result. One, a recurrent sarcoma of the front of the thigh, nearly disappeared and I removed it; but the man came back in less than a year with metastasis in the orbit. In two cases of recurrent sarcoma of the muscles of the thigh and of the nose respectively, both got slightly smaller, but the latter patient subsequently died.

In his paper before this Society in 1909,<sup>1</sup> Coley gives his results in nine selected cases of sarcoma of the long bones, in all of which the tumour disappeared. Two cases of periosteal sarcoma of femur in which no operation was performed—one well after seven years, and one died of metastasis one year later. Three cases of periosteal sarcoma of femur treated by amputation—all well after three years. A spindle-celled sarcoma of the tibia, recurrent after excision; it disappeared under toxins, and the patient was well ten years later. He also quotes three cases of myeloma which disappeared; of these, two were well four years, and the other one year after their disappearance. Two of them were not operated on.

At the London Hospital we have treated five cases of periosteal sarcoma without the slightest result on the tumour. Three patients were lost sight of, one died within a year, one, with periosteal sarcoma of the lower end of the femur, is well two years and five months after a hip-joint amputation. In this case and another case of round-celled chondro-sarcoma of the tibia, treatment was carried out most thoroughly in my wards with toxin kindly sent by Dr. Coley.

My own experience as regards the prevention of recurrence by Coley's fluid has been most disappointing. For it happens that, in the

<sup>1</sup> *Proceedings*, 1910, iii, pp. 1-44.

only three cases in which I have seen a striking diminution of the tumour, but where local removal was subsequently performed as freely as circumstances would permit, in two local recurrence took place, and in one (already mentioned) metastasis.

It is undeniable that a certain number of sarcomata disappear or are profoundly influenced by the toxins, but we have no means of determining what proportion this is to the total number treated. I suspect it is only a small proportion.

Although I may be forming an opinion on insufficient evidence, yet my present attitude is, that I would not recommend Coley's fluid in any case of operable sarcoma, nor would I recommend it as a prophylactic against recurrence.

Mr. E. W. HEY GROVES (Bristol) said he wished to offer a few remarks on the general principles of the subject under discussion, and to illustrate his remarks by descriptions of three cases. The first case had particular reference to what Sir John Bland-Sutton had said on the question of endotheliomata on bone, and on which Sir Frederic Eve spoke—namely, their treatment by grafting. The specimen was one of endothelioma of the ulna, and he handed round two skiagrams of the condition before operation. It was a growth secondary to a nævus of the scalp; the nævus recurred, and its recurrence was recognized to be endotheliomatous. The next symptom was a tumour of the ulna, which was completely resected, including the diaphysis, without amputation, and a graft from the anterior border of the tibia was put in, being supported in its place by a steel strut. He did well for nine months, the arm functioning very well, but he died of metastasis in the chest. One of the other cases was an almost unique instance of multiple myelomata, the patient also having albumosuria. With regard to the pathology of sarcomata, his observations would tend to confirm what had just been said as to the possibility that myelomata might sometimes undergo actual arrest—i.e., their existence might be compatible with an almost indefinite prolongation of life. These skiagrams, which included myelomata of metacarpal bones, tibia, femur, os calcis, radius, ulna and humerus, were from a man aged 39, who, for five years, 1902-07, was constantly developing these tumours with spontaneous fractures. Probably during the whole of that time he had albumosuria as well. But the interesting fact was that, unlike any other recorded case of the disease, the man did not die, and since 1907 he had remained in much the

same condition, although, of course, very much crippled. Every limb had been the seat of one or two tumours and fractures, but his health seemed now to be good; and if these were myelomata, as he supposed they must be, it must be a good example of those tumours having come to a standstill. His last case seemed to bring out a very practical and important point in treatment. He was rather surprised to hear Sir Frederic Eve speak of the treatment of sarcomata of long bones as a threadbare garment about which there was very little fresh to be done. Sir Frederic himself falsified that statement by proceeding to say a good many new and interesting things about the treatment. A point of enormous practical importance was, in what cases was one bound to amputate for sarcoma, and in what cases was one justified in merely resecting? He ventured respectfully to suggest that the evidence in favour of the amputation of limbs for sarcomata had very little clinical support. He showed two photographs from a girl, aged 13, with periosteal sarcoma. A forequarter amputation having been refused, it was treated merely by resection or erosion, and now, rather more than two years after the operation, she was alive and well. He did not suggest that this was unique: Sir Frederic Eve himself mentioned several cases of spindle-celled sarcomata which were alive several years after that partial operation. Of course, it was well known that amputation for sarcomata was frequently followed by death after a very short period of time, and he suggested that it was very much open to question whether one was ever justified in advising a big amputation for sarcoma. In certain types of malignancy—and one could not tell beforehand which were the extremely malignant types—however big the operation performed, recurrence and death ensued six months or so afterwards. But there were others in which local removal was satisfactory, and the life was preserved for many years afterwards. In the case of which he was speaking the girl came to the hospital and was under the care of one of his colleagues. Her parents were told that the only operation which was justifiable was amputation, including the clavicle and scapula. The parents refused to have this done, and as his colleague was leaving for his holiday the case came under his (the speaker's) care. As the parents had assumed the responsibility of refusing the suggested operation, he thought it was worth while trying local treatment. The tumour was accordingly removed, and was reported by the pathologist to be a mixed-celled sarcoma, and certainly not a myeloma. His impression was that she would certainly have a quick recurrence. He was astonished to find, however, not only that it healed, but that she had survived and

was now in perfect health. That case was not unique, and it showed that it was high time that the records of cases of this kind should be considered together, and the old-fashioned doctrine that periosteal sarcoma, or any of the myeloid sarcomata, could only be treated by high amputation, should be seriously challenged.

Mr. R. C. ELMSLIE said he thought that in this discussion one started with the presumption that sarcoma of the long bones, at least the periosteal variety, was a fatal disease, in which the diagnosis was very difficult, often uncertain, and the established treatment at present was very drastic and maiming; and that, even after that treatment, the prognosis was very bad. Therefore it was necessary to take the greatest possible care in making a certain diagnosis. There were two points in particular in connexion with their diagnosis which he would bring forward. In the case of true periosteal sarcoma of the femur or of any part, he felt that at best one could only do a rather wide amputation or removal of the bone, which often left a useless limb; and even then the prognosis was so bad that this radical operation should be reserved for cases in which the diagnosis had been definitely proved.

With regard, first, to endosteal growths. If one excluded myeloid sarcomata, tumours which were sarcomata and which were diagnosable as truly endosteal, surrounded by a shell of bone and not bursting through at any point, were excessively rare. And tumours other than sarcomata, as Sir John Bland-Sutton had said, if not common, certainly did occur. He had a collection of skiagrams of different endosteal tumours, which he had collected for several years. The collection included only one true endosteal sarcoma. Its nature could be seen from the skiagram, as its shell of bone was incomplete, so that the tumour had burst through and was infiltrating beyond, and he handed round for comparison the skiagram of a typical myeloma. Of other endosteal tumours, the first was the cold abscess, which showed a clear space in the bone with, in this case, no periosteal formation of new bone, a point which needed emphasis in diagnosis. He diagnosed it as a cyst with great confidence, but when it was opened pus was found inside. The next group of which he had specimens were benign cysts in long bones, to which Sir John Bland-Sutton had alluded. He had illustrations of three cases, all cysts of the humerus, occurring in identical situations. All were in boys, who came to the hospital because of spontaneous fracture, the cyst being revealed by the skiagram. He would say a little more about these cysts, because he differed from

Sir John Bland-Sutton on an important point. He thought it was possible in the majority of cases confidently to diagnose cysts from myelomata by the clinical signs and by the skiagrams. Cysts were not in the epiphyses, but were on the distal side of the epiphyseal line. They occurred most commonly in certain definite situations—upper end of shaft of humerus, upper end of shaft of femur, and in the tibia—and there was, except in rare cases of old standing, little or no expansion of bone. And in a cyst, before any accident had occurred to it, there was no division of the clear space by trabeculae. After a fracture and its healing, this trabeculation appeared. He exhibited a skiagram showing the tumour after fracture now resembling myeloid sarcoma, not occurring, however, in the epiphysis, but some distance down the diaphysis. Cysts, also, were practically always centrally situated, a diagnostic point against other tumours. There was a bony shell which was complete, until fracture occurred. He showed a skiagram of a cyst two and a half years after it had been opened and curetted, disclosing a small persistent cystic space. The next group of endosteal tumours which might cause difficulties in diagnosis were the cases known as fibrous osteitis. He showed a skiagram of such a case in the upper end of the femur; there was a close resemblance to the appearance of myeloid sarcoma. He would probably have diagnosed it as the latter but for the fact that he saw the patient in 1907, and knew that the condition had dated back to 1880, when he found the patient had been in one of the wards of St. Bartholomew's Hospital. There were other inflammatory endosteal tumours, such as gummata and other new growths. He showed a skiagram of enchondroma of the upper end of the humerus, and one showing two enchondromata of the fibula. Further, there were secondary growths, particularly secondary carcinomata; to illustrate these he showed a skiagram of secondary thyroid tumour. To those he must now add, after what had been said at this meeting, endothelioma, perithelioma, and naevus. His point was that if an endosteal tumour, which was expanding the bone but had not burst through at any point, was discovered in a patient it should be presumed to be innocent or secondary, and not a sarcoma, until there was proof to the opposite; and a radical operation should not be undertaken until that tumour had been explored and its nature ascertained with certainty. The second point in diagnosis was, that an exploratory incision should be made with a microscopist present at the time of the operation. In this matter he had had the advantage of four or five years' experience in



the pathological department of his hospital, where he undertook the cutting of sections himself, and he wished to say a few words about the mistakes which occurred in certain cases of exploratory incision. In the Museum at St. Bartholomew's there were two specimens of very great interest and importance. Each was a femur containing a patch of necrosis, and a large mass of inflammatory new periosteal bone around. Each of them was amputated under the impression that it was sarcoma, after exploratory incision into the tumour. They occurred before the days of skiagraphy; nowadays, no doubt, a good skiagram would lead to the diagnosis being made. In these two cases the exploratory incision failed because it was not carried deep enough. Mr. Ernest Shaw, who had had a large experience of the subject, would speak later on the difficulties of diagnosis from microscopical sections. He wished to assert that the majority of mistakes and failures after exploratory incision were due to the surgeon not cutting deep enough, or else not cutting into the right part. One such case occurred to him. He was in the theatre to cut sections for a surgeon in the case of a boy with chronic enlargement of the knee-joint, which enlargement had been present for two months. There was no tumour clearly to be felt at the knee-joint, and the diagnosis was uncertain, lying between tuberculous disease of the joint and early sarcoma of the lower end of the femur. Incision was made into the joint and some synovial membrane was given to him to cut. He cut several sections of it, but found only chronic inflamed synovial membrane, and he reported that there was no tubercle. Amputation was carried out through the lower part of the shaft of the femur, and on examining the femur at its lower end afterwards, a sarcoma was found in the periosteum. The exploratory incision had been carried into the wrong part. It was very important that surgeons should make such incisions deep enough, and, if possible, they should have a pathologist at their elbow and allow him some small say in the determination of the part to be examined.

(The discussion was adjourned until November 19.)



## **Surgical Section.**

November 19, 1912.

MR. G. H. MAKINS, C.B., President of the Section, in the Chair.

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### **A Discussion on Sarcomata and Myelomata of the Long Bones.<sup>1</sup>**

#### **OPENING ADDRESS WITH REGARD TO PROGNOSIS.**

MR. G. E. GASK said it was impossible to come before such a meeting and discuss the prognosis of sarcomata of long bones without having at least a few facts to place before his hearers. Therefore he had traced, as well as he was able, the after-histories of all cases of sarcoma of long bones which occurred at St. Bartholomew's Hospital during the years 1902-11. In starting those tables, he confessed that the idea of separating them into groups of the traditional character—namely, periosteal and endosteal—did not hold, for he soon found he was unable to do that, because, whether from reference to the notes or to the museum specimens, he often completely failed to satisfy himself whether they started inside the bone, or from the periosteum, or from the subperiosteal tissue. He therefore had recourse to the microscopical examination, and the cases had been divided into two main groups: (1) Those which, by microscopical examination, satisfied the Pathological Department during the last ten years that they were definitely myeloid sarcoma; (2) all the other forms of sarcoma, whether round-, spindle-, or mixed-celled, or mixed with cartilage or bone. In order to compare these results, he had placed them alongside those from the late Sir

<sup>1</sup> Second meeting (adjourned from November 12).

Henry Butlin's book on the "Operative Surgery of Malignant Disease," which went up to the year 1900. Throwing out doubtful cases, the number of cases he had collected was sixty-one. Those figures agreed closely with the figures found in Mr. Andrew's book on "Age Incidence, Sex and Comparative Frequency of Disease." Comparing his own figures with Butlin's brought out one striking fact—namely, that the mortality of those cases owing to operation had dropped to *nil*. Sir Henry Butlin foresaw this, and stated in his book that with asepsis and care in all probability the mortality would very rapidly decrease. Next—to take the brighter side first—it would be seen that in myeloid tumours three cases occurred in the tibia in St. Bartholomew's Hospital. One was lost sight of, one was alive and well between two and three years after, and one was alive and well ten years later. Though the figures, on the whole, were small, they looked favourable. Of two cases of sarcoma of the radius, one had recurrence after two months, and was then lost sight of. Another was alive after three years. Of Butlin's figures, one patient died after operation, some were lost sight of, one died of recurrence, while six were well more than three years afterwards. In connexion with the periosteal type there was a different story, though the results were still very bad. Of twenty-one cases at St. Bartholomew's Hospital during ten years, there died of recurrence or metastasis sixteen. Of Butlin's sixty-eight, twelve died of operation, fourteen were lost sight of, eleven had recurrence, thirteen had metastasis, while four were well from one to two years afterwards. A similar story had to be told in connexion with periosteal tumour of the tibia, except that at St. Bartholomew's Hospital one patient was well five years afterwards. It was an even more dismal record in regard to the humerus, for of eight cases occurring in the ten years not one had survived. He tried, incidentally, to find out whether those who had no operation done survived longer than those who were operated upon, but he was unable to satisfy himself about this. Three cases of sarcoma of humerus with no operation died. Sarcoma of the scapula showed figures which were rather peculiar, for most of the patients died within a short period of the operation; but one patient at St. Bartholomew's Hospital was alive and well four years afterwards, and one of Butlin's was alive and well six years afterwards. He had also tried to ascertain whether removal of the lymphatic glands had any influence on the prognosis, but he was unable to establish anything, because the records on the matter were not complete. But in one or two instances there was definite proof that the lymphatic glands were

infected with sarcoma at the time of the operation. Another point was the effect of injury of the limb before the recognition of sarcoma. Of sixty-one cases there was a history of injury in thirteen; but usually the history was so vague that he did not think any accurate deductions could be made from it.

He next wished to deal with those sarcomata, which were mixed with cartilage. He had had the impression for some years that the cases of sarcoma of bones which had cartilage in them were less malignant than were any other kind of sarcoma except myeloid. Therefore he had gathered from the list the cases in which microscopical examination showed a mixture of cartilage cells. But the number of such cases was so few that he would rather postpone that point for further consideration.

In conclusion, he thought that from these tables one might arrive at the following points: (1) That the mortality due to the operation was very small; (2) the prognosis of myeloid sarcoma was good, particularly after amputation. A certain number of cases recurred, and amputation had to be done subsequently. With regard to periosteal sarcoma, using that term in the broad sense, the prognosis was still terribly bad; and he submitted that if the prognosis was to be improved the diagnosis must be made even earlier than was at present the case. A diagnosis could only be made by an incision, and by microscopical section. He would go further and say that a prognosis could only be given after a microscopical examination. It would be most useful to see the results in the next ten years with earlier diagnosis, a freer removal of the disease, and a free removal of the lymphatic glands. It was to be hoped that the result would be a better series of figures than could be produced for the past ten years.

Table of the Results of Treatment of Sarcoma of the Long Bones, including the Clavicle, Femur, Fibula, Humerus, Radius, Scapula, and Tibia. Treated at St. Bartholomew's Hospital during the period of Ten Years 1902-1911.

By G. E. GASK, F.R.C.S.

SARCOMA OF CLAVICLE.

| No. of case | Sex | Age | Operation  | Result   | Cause of death | Microscopic examination    | Site of growth | History of injury | Remarks   |
|-------------|-----|-----|--|--|----------------|----------------------------|----------------|-------------------|---|
| 33          | F.  | 30  | Excision of inner end of clavicle  | Alive and well 18 months after operation   | —              | Chondro-sarcoma (doubtful) | Inner end      | None              | It seems doubtful whether this was really a case of sarcoma |
| 38          | F.  | 21  | Partial excision of clavicle; 9 months later removal of remainder of clavicle; 11 months later removal of cervical gland | Lost sight of; no trace of death entry in Registrar-General's Returns up to 7½ years after operation | —              | Mixed-celled sarcoma       | Inner end      | None              | —   |

SARCOMA OF FEMUR.

|   |    |    |                                   |   |          |   |                                |      |                    |
|---|----|----|-----------------------------------|---|----------|---|--------------------------------|------|--------------------|
| 1 | M. | 38 | Amputation upper third of thigh   | Alive and well 18 months after operation; no recurrence | —        | Large round- and spindle-celled sarcoma | Lower end                      | None | Glands not removed |
| 5 | M. | 26 | Amputation below great trochanter | Died 11 months after operation                          | Pleurisy | Round-celled sarcoma                    | Lower end, invading knee-joint | None | Glands removed     |



SARCOMA OF FEMUR—(continued).

| No. of case | Sex | Age | Operation   | Result   | Cause of death  | Microscopic examination                                       | Site of growth | History of injury  | Remarks  |
|-------------|-----|-----|---|--|---|---|----------------|--------------------|--|
| 37          | F.  | 41  | Amputation, lower third of thigh  | Died 4 years 2 months after operation  | Not ascertained   | Spindle-celled sarcoma  | Lower end      | None               | One year previous the knee-joint had been excised for tuberculosis |
| 40          | F.  | 13  | Amputation, middle of thigh   | Died 6 months after operation  | Not ascertained   | Mixed-celled sarcoma  | Lower end      | None               | Glands enlarged  |
| 44          | F.  | 26  | Amputation, middle of thigh; 6 months later amputation through hip-joint for local recurrence | Died 15 months after operation   | Acute phthisis and asthenia                                   | Osteoid sarcoma   | Lower end      | None               | Glands not mentioned   |
| 45          | F.  | 31  | Operation refused   | No trace of death entry in Registrar-General's Returns up to 8 years after admission | —   | —   | Lower end      | History of a blow  | Diagnosed as a periosteal sarcoma                                  |
| 48          | M.  | 37  | Amputation, middle of thigh   | Alive and well 10 years after operation  | —   | Myeloid sarcoma   | Lower end      | History of a fall  | —  |
| 57          | M.  | 26  | Amputation, upper third of thigh  | Died 9 months after operation  | Local recurrence  | Spindle-celled sarcoma; a few multi-nucleate giant cells also | Lower end      | None               | Glands not mentioned   |
| 55          | M.  | 15  | Amputation, upper third of thigh  | Died 3 months after operation  | Recurrence in lung  | Myxo-sarcoma  | Lower end      | History of fall    | Glands not mentioned   |
| 68          | M.  | 9   | Amputation through hip-joint  | Alive and well 12 months after operation   | —   | Myeloid sarcoma   | Lower end      | None               | Glands not enlarged  |
| 69          | M.  | 7   | Operation refused   | Died 10 months after admission   | Deposits in liver and lungs; asthenia                         | —   | Lower end      | None               | Diagnosed as periosteal sarcoma                                    |
| 70          | F.  | 32  | Amputation through hip-joint  | Died 4 months after operation  | Recurrence in pelvis and lumbar vertebrae                     | Round-celled sarcoma  | Upper end      | History of a knock | —  |
| 73          | M.  | 37  | Amputation, upper third of thigh  | Died 4 months after operation  | Recurrence in stump and glands; deposits in lungs; hæmoptysis | Small round-celled sarcoma                                    | Lower end      | None               | —  |

## SARCOMA OF FIBULA.

| 3 | M. | 17 | Amputation of thigh (Stokes-Gritti) | Alive and well 15 months after operation; no recurrence | — | Small round-celled sarcoma with hyaline cartilage | Upper end | None |
|---|----|----|-------------------------------------|---|---|---|-----------|------|
|---|----|----|-------------------------------------|---|---|---|-----------|------|

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## SARCOMA OF HUMERUS.

|    |    |    |                                   |                                |  |  |                                       |   |  |
|----|----|----|-----------------------------------|--------------------------------|--|--|---------------------------------------|---|--|
| 3  | M. | 17 | Interscapulo-thoracic amputation  | Died 8 months after operation  | Recurrence in neck, and cough                                  | Mixed-celled sarcoma                       | Upper end                             | History of strain                       | Spontaneous fracture; no mention of glands   |
| 10 | M. | 56 | Amputation through shoulder-joint | Died 6½ months after operation | Paraplegia   | Mixed-celled sarcoma and calcifying stroma | Lower end                             | None                                    | Osteitis deformans; Museum, 72 E 1   |
| 46 | M. | 50 | Amputation through shoulder-joint | Died 3 months after operation  | Secondary growths in lung; muscular atrophy                    | Mixed-celled sarcoma of alveolar type      | Shaft of humerus                      | None                                    | Spontaneous fracture   |
| 53 | M. | 32 | Operation refused                 | Died 18 months after admission | Not ascertained  | —  | Involving the whole extent of humerus | None                                    | The swelling had been noticed 18 years; an attempt at local removal made 16 years ago at Newcastle; diagnosis, chondro-sarcoma |
| 58 | F. | 17 | Amputation through shoulder-joint | Died 9 months after operation  | Not ascertained  | Spindle-celled calcifying sarcoma          | Upper end                             | None                                    | —  |
| 60 | M. | 37 | Regarded as inoperable            | Died                           | Not ascertained  | —  | Upper end of humerus involving joint  | None                                    | Glands enlarged  |
| 63 | M. | 63 | Regarded as inoperable            | Died 6 months after admission  | Asthenia   | —  | Upper end                             | Swelling noticed 1 year after an injury | —  |
| 71 | M. | 16 | Interscapulo-thoracic amputation  | Died 5 months after operation  | Secondary deposits in skull, heart, lungs, liver and vertebrae | Spindle-celled sarcoma                     | Upper end                             | None                                    | —  |



## SARCOMA OF RADIUS.

| No. of Case | Sex | Age | Operation                        | Result  | Cause of death  | Microscopic examination | Site of growth | History of injury | Remarks   |
|-------------|-----|-----|----------------------------------|---|---|-------------------------|----------------|-------------------|---|
| 4           | M.  | 25  | Enucleation                      | Recurred 2 months later                         | Lost sight of; no trace of death entry in Registrar-General's Returns | Myeloid sarcoma         | Lower end      | History of sprain | —   |
| 8           | M.  | 27  | Removal of lower third of radius | Alive and well 3 years 4 months after operation | —   | Myeloid sarcoma         | Lower end      | A vague history   | Loss of lower end of radius is a terrible deformity |

## SARCOMA OF SCAPULA.

|    |    |    |                                  |  |   |                            |                           |      |                                   |
|----|----|----|----------------------------------|--|---|----------------------------|---------------------------|------|-----------------------------------|
| 9  | M. | 64 | Interscapulo-thoracic amputation | Died 2½ months after operation                                 | Secondary deposits in lungs; pleural effusion | Osteo-chondro-sarcoma      | —                         | None | Glands not mentioned              |
| 12 | M. | 11 | Excision of blade of scapula     | Alive and well 4 years after operation                         | —   | Alveolar sarcoma           | Blade of scapula          | None | Glands removed                    |
| 24 | M. | 70 | Excision of blade of scapula     | Died 16 months after operation                                 | Bronchitis                                    | —                          | Blade of scapula          | None | Glands not mentioned              |
| 26 | M. | 25 | Interscapulo-thoracic amputation | Died 3½ months after operation                                 | Not ascertained                               | Large round-celled sarcoma | —                         | None | Glands removed and found infected |
| 29 | M. | 47 | Excision of scapula              | Died 4 months after operation                                  | Chronic cystitis and exhaustion               | Mixed-celled sarcoma       | —                         | None | Glands not removed                |
| 35 | F. | 8  | Operation refused                | Two years later the tumour is larger and the child wasted      | —   | —                          | —                         | None | Tumour noticed since birth        |
| 47 | M. | 24 | Partial removal of scapula       | Local recurrence 2 months later; died 4 months after operation | Not ascertained                               | Round-celled sarcoma       | Lower end of left scapula | None | Glands enlarged                   |

|    |    |    |                                  |  |                 |                  |                                       |                                 |
|----|----|----|----------------------------------|--|-----------------|------------------|---------------------------------------|---------------------------------|
| 67 | M. | 2½ | Incision -- found inoperable     | Twelve months later shows a growth in thigh and spontaneous fracture | Not ascertained | Blade of scapula | None                                  | Diagnosed as periosteal sarcoma |
| 75 | F. | 42 | Interscapulo-thoracic amputation | Died 4 weeks later   |                 |                  | History of injury 3 months previously |                                 |

## SARCOMA OF TIBIA.

|    |    |    |  |   |                      |                 |           |                              |   |
|----|----|----|--|---|----------------------|-----------------|-----------|------------------------------|---|
| 13 | M. | 67 | Amputation lower third of thigh                  | Died 12 months after operation  | Recurrence in "head" | Fibro-sarcoma   | Upper end | None                         | Spontaneous fracture; glands not removed                          |
| 15 | M. | 34 | Amputation lower third of thigh                  | Lost sight of; no trace of death entry in Registrar - General's Returns up to 4 years after operation |                      | Chondro-sarcoma | Upper end | None                         | Glands not removed  |
| 19 | M. | 12 | Amputation lower third of thigh                  | Alive and well 5 years after operation; no recurrence   |                      | Myxo-sarcoma    | Upper end | None                         | No mention of glands  |
| 23 | M. | 58 | Refused operation                                | Lost sight of; no trace of death entry in Registrar - General's Returns up to 4 years after admission |                      |                 | Upper end | A definite history of a blow |   |
| 27 | M. | 19 | Amputation lower third of thigh                  | Died 11 months after operation  | Recurrence in lung   |                 | Upper end | None                         | Glands enlarged, but not removed; diagnosed as periosteal sarcoma |
| 28 | M. | 51 | Local removal; later amputation, middle of thigh | Lost sight of; no trace of death entry in Registrar - General's Returns up to 7 years after operation |                      | Myeloid sarcoma | Upper end | History of blow              | Glands not removed  |

## SARCOMA OF TIBIA—(continued).

| No. of Case | Sex Age | Operation  | Result  | Cause of death                      | Microscopic examination                       | Site of growth | History of injury | Remarks   |
|-------------|---------|--|---|-------------------------------------|---|----------------|-------------------|---|
| 32          | F. 19   | Amputation lower third of thigh  | Alive and well 3 months after operation   | —                                   | Mixed-celled sarcoma                          | Upper end      | None              | Glands not mentioned  |
| 36          | F. 19   | Local excision   | Died 2 years 9 months after operation   | Not ascertained                     | Chondro-sarcoma with spindle cells            | Upper end      | None              | Glands not removed  |
| 41          | F. 16   | Local removal  | Alive and well; no recurrence 10½ years after operation   | —                                   | Myeloid sarcoma                               | Upper end      | History of a fall | Movements of knee perfect; no hindrance of growth of bone       |
| 42          | F. 15   | Local removal; amputation lower third of thigh 6 months later for recurrence | Lost sight of; no trace of death entry in Registrar - General's Returns up to 9 years after operation | —                                   | Mixed-celled sarcoma                          | Upper end      | None              | No mention of glands  |
| 49          | M. 49   | Amputation middle third of thigh   | Lost sight of; no trace of death entry in Registrar - General's Returns up to 8 years after operation | —                                   | Mixed-celled sarcoma, stated to be periosteal | Upper end      | None              | No enlarged glands found  |
| 50          | M. 68   | Amputation middle third of thigh   | Died 3 days after leaving hospital  | Not ascertained                     | Mixed-celled sarcoma                          | Upper end      | None              | The growth was ulcerated and bleeding; inguinal glands enlarged |
| 52          | M. 36   | Amputation middle third of thigh   | Alive and well 2½ years after operation   | —                                   | Myeloid sarcoma                               | Upper end      | None              | —   |
| 72          | M. 65   | Amputation middle of thigh   | Died 6 days after operation   | Dilatation of heart; œdema of lungs | Spindle-celled sarcoma                        | Upper end      | None              | —   |

## SYNOPSIS OF TABLES.

## ST. BARTHOLOMEW'S HOSPITAL CASES DURING THE TEN YEARS 1902-1911.

| Bone affected   | Male | Female | Total |
|-----------------|------|--------|-------|
| Clavicle ... .. | 0    | 2      | 2     |
| Femur ... ..    | 18   | 7      | 25    |
| Fibula ... ..   | 1    | 0      | 1     |
| Humerus ... ..  | 7    | 1      | 8     |
| Radius ... ..   | 2    | 0      | 2     |
| Scapula ... ..  | 7    | 2      | 9     |
| Tibia ... ..    | 10   | 4      | 14    |
| Ulna ... ..     | 0    | 0      | 0     |
| Total ... ..    |      |        | 61    |

*Sarcoma of Clavicle. St. Bartholomew's Hospital.*

|   |   |
|---|---|
| Alive and well 18 months after operation ... .. | 1 |
| Recurred twice, and then lost sight of ... ..   | 1 |
| Total ... ..                                    | 2 |

*Butlin's Figures of Sarcoma of Clavicle (all described as Cases of Periosteal Sarcoma).*

|                                       |   |
|---------------------------------------|---|
| Rapid recurrence ... ..               | 3 |
| Died a few days after ... ..          | 1 |
| Lost sight of ... ..                  | 1 |
| Alive and well 2½ months after ... .. | 1 |
| Alive and well 5 months after ... ..  | 1 |
| Total ... ..                          | 7 |

*Sarcoma of Femur (Sarcoma of a Type other than Myeloid). St. Bartholomew's Hospital.*

|   |    |
|---|----|
| Died of operation ... ..                          | 0  |
| Died of either recurrence or of metastasis ... .. | 16 |
| Died of intermittent malady (?) ... ..            | 1  |
| Lost sight of ... ..                              | 3  |
| Alive and well 18 months after operation ... ..   | 1  |
| Total ... ..                                      | 21 |

*Butlin's Figures of Periosteal Sarcoma of Femur.*

|  |    |
|--|----|
| Died of the operation ... ..                           | 12 |
| Lost sight of ... ..                                   | 14 |
| Dead or alive with recurrence ... ..                   | 11 |
| Dead or alive with metastasis ... ..                   | 13 |
| Dead of either recurrence or metastasis ... ..         | 11 |
| Well 7 months after operation ... ..                   | 1  |
| Well from 1 to 2 years ... ..                          | 4  |
| Died of uncertain cause 3 years after operation ... .. | 1  |
| Well 8 years after operation ... ..                    | 1  |
| Total ... ..   | 68 |

## 72 Gask: *Sarcomata and Myelomata of Long Bones*

### *Sarcoma of Femur (the Myeloid Type). St. Bartholomew's Hospital.*

|                                      |          |
|--------------------------------------|----------|
| Died of operation ... ..             | 0        |
| Lost sight of ... ..                 | 1        |
| Alive and well 1 year after ... ..   | 1        |
| Alive and well 4½ years after ... .. | 2        |
| Alive and well 10 years after ... .. | 1        |
| <b>Total</b> ... ..                  | <b>5</b> |

### *Butlin's Figures of Central Sarcoma of Femur.*

|                                      |           |
|--------------------------------------|-----------|
| Died of the operation ... ..         | 11        |
| Lost sight of ... ..                 | 18        |
| Dead or alive with recurrence ... .. | 2         |
| Dead of metastasis ... ..            | 5         |
| Dead soon, of unknown cause ... ..   | 2         |
| Well 9 months later ... ..           | 1         |
| Well from 1 to 2 years later ... ..  | 2         |
| Well more than 3 years later ... ..  | 5         |
| <b>Total</b> ... ..                  | <b>46</b> |

### *Sarcoma of Humerus. St. Bartholomew's Hospital.*

Eight cases recorded and all were of the "periosteal" type.

|   |          |
|---|----------|
| Died of the operation ... ..                    | 0        |
| Died with recurrence or metastasis ... ..       | 4        |
| Died, no operation having been performed ... .. | 3        |
| Died, cause of death unknown ... ..             | 1        |
| <b>Total</b> ... ..                             | <b>8</b> |

### *Sarcoma of Radius. St. Bartholomew's Hospital.*

Two cases recorded, both of the myeloid type.

|  |          |
|--|----------|
| Recurrence after 2 months, then lost sight of ... .. | 1        |
| Alive and well over 3 years after ... ..             | 1        |
| <b>Total</b> ... ..                                  | <b>2</b> |

### *Butlin's Figures of Central Sarcoma of Radius and Ulna.*

|                               |           |
|-------------------------------|-----------|
| Died of the operation ... ..  | 1         |
| Lost sight of ... ..          | 5         |
| Died of recurrence ... ..     | 1         |
| Well from 1 to 2 years ... .. | 1         |
| Well from 2 to 3 years ... .. | 2         |
| Well more than 3 years ... .. | 6         |
| <b>Total</b> ... ..           | <b>16</b> |

### *Sarcoma of Scapula. St. Bartholomew's Hospital.*

Nine cases recorded—all diagnosed as of the periosteal type.

|   |          |
|---|----------|
| Died of the operation ... ..              | 0        |
| Dead with recurrence or metastasis ... .. | 2        |
| Died soon after, cause uncertain ... ..   | 4        |
| Alive but unrelieved—no operation ... ..  | 2        |
| Alive and well 4 years after ... ..       | 1        |
| <b>Total</b> ... ..                       | <b>9</b> |

*Butlin's Figures (Poinso) of Sarcoma of Scapula.*

|                                       |     |     |     |     |     |    |
|---------------------------------------|-----|-----|-----|-----|-----|----|
| Died of the operation                 | ... | ... | ... | ... | ... | 2  |
| Died shortly after ...                | ... | ... | ... | ... | ... | 2  |
| Dead or alive with recurrence         | ... | ... | ... | ... | ... | 11 |
| Amputation for recurrence             | ... | ... | ... | ... | ... | 1  |
| Spoken of as "cured"—duration unknown | ... | ... | ... | ... | ... | 4  |
| Remaining well after 18 months        | ... | ... | ... | ... | ... | 1  |
| Alive and well 6 years after          | ... | ... | ... | ... | ... | 1  |
| Lost sight of                         | ... | ... | ... | ... | ... | 3  |
| Total                                 | ... | ... | ... | ... | ... | 25 |

*Sarcoma of Tibia. St. Bartholomew's Hospital.*

|                                  |     |     |     |     |     |    |
|----------------------------------|-----|-----|-----|-----|-----|----|
| Died of the operation            | ... | ... | ... | ... | ... | 0  |
| Died 6 days after ...            | ... | ... | ... | ... | ... | 1  |
| Lost sight of                    | ... | ... | ... | ... | ... | 4  |
| Died of recurrence or metastasis | ... | ... | ... | ... | ... | 2  |
| Died, cause unknown              | ... | ... | ... | ... | ... | 2  |
| Alive and well 3 months after    | ... | ... | ... | ... | ... | 1  |
| Alive and well 5 years after     | ... | ... | ... | ... | ... | 1  |
| Total                            | ... | ... | ... | ... | ... | 11 |

*Butlin's Figures of Periosteal Sarcoma of Tibia.*

|                                       |     |     |     |     |     |    |
|---------------------------------------|-----|-----|-----|-----|-----|----|
| Died of the operation                 | ... | ... | ... | ... | ... | 1  |
| Lost sight of                         | ... | ... | ... | ... | ... | 13 |
| Dead or alive with recurrence         | ... | ... | ... | ... | ... | 3  |
| Died of metastasis...                 | ... | ... | ... | ... | ... | 11 |
| Died soon after (probably metastasis) | ... | ... | ... | ... | ... | 2  |
| Well from 1 to 2 years                | ... | ... | ... | ... | ... | 4  |
| Well 7 years later                    | ... | ... | ... | ... | ... | 1  |
| Total                                 | ... | ... | ... | ... | ... | 35 |

*Sarcoma of Tibia. St. Bartholomew's Hospital.**Three cases recorded of the myeloid type.*

|                               |     |     |     |     |     |   |
|-------------------------------|-----|-----|-----|-----|-----|---|
| Died of the operation         | ... | ... | ... | ... | ... | 0 |
| Lost sight of                 | ... | ... | ... | ... | ... | 1 |
| Alive and well 2 to 3 years   | ... | ... | ... | ... | ... | 1 |
| Alive and well 10 years after | ... | ... | ... | ... | ... | 1 |
| Total                         | ... | ... | ... | ... | ... | 3 |

*Butlin's Figures of Myeloid Sarcoma of Tibia.*

|  |     |     |     |     |     |    |
|--|-----|-----|-----|-----|-----|----|
| Died of the operation                        | ... | ... | ... | ... | ... | 9  |
| Lost sight of                                | ... | ... | ... | ... | ... | 19 |
| Died within a year of other or unknown cause | ... | ... | ... | ... | ... | 4  |
| Died of recurrence or metastasis             | ... | ... | ... | ... | ... | 2  |
| Well from 1 to 2 years                       | ... | ... | ... | ... | ... | 7  |
| Well from 2 to 3 years                       | ... | ... | ... | ... | ... | 2  |
| Well more than 3 years                       | ... | ... | ... | ... | ... | 9  |
| Total  | ... | ... | ... | ... | ... | 52 |

## 74 Reid: *Sarcomata and Myelomata of Long Bones*

*Sarcomata with Admixture of Cartilage.—Four Cases. St. Bartholomew's Hospital.*

| Bone affected  | Operation                           | Microscopic examination                           | Result  |
|----------------|-------------------------------------|---|---|
| (1) Tibia ...  | Amputation of thigh; lower third    | Chondro-sarcoma                                   | Lost sight of; no trace of death entry in Registrar-General's Returns up to 4 years after operation |
| (2) Tibia ..   | Local excision                      | Chondro - sarcoma with spindle cells              | Died 2½ years after; cause of death not ascertained   |
| (3) Femur ...  | Amputation of thigh; upper third    | Chondro-sarcoma                                   | Died 4 years 8 months after; acute pulmonary tuberculosis   |
| (4) Fibula ... | Amputation of thigh (Stokes-Gritti) | Small round-celled sarcoma with hyaline cartilage | Alive and well 13 months after operation  |

### INTRODUCTORY ADDRESS WITH REGARD TO X-RAY APPEARANCES.

Mr. ARCHIBALD D. REID: The value of the X-ray examination in sarcomata and myelomata of the long bones is naturally in direct ratio to the duration of the condition. It is exceptional that the symptoms are sufficient to call for examination in the very early stages, and consequently the majority of the cases seen show abnormalities of a more or less definite description in the X-ray plate. It is with these abnormalities that I have to deal, and I propose briefly to give the details of these appearances.

Periosteal sarcoma (non-ossifying type) only shows alteration in the bone of an eroding type, no new bone being laid down. This appearance is not diagnostic in itself, because other conditions can simulate it.

Periosteal sarcoma (ossifying type) in the early stage generally starts from a limited area of the bone, and even in the very early stages in a good skiagram the peculiar arrangement of the growth can be detected. The characteristic feature is the spicular arrangement of the periosteal growth which is at right angles to the shaft. This condition is practically pathognomonic. When the disease has progressed further the growth may completely surround the bone and very dense masses may be seen, which are still more or less arranged radiating from the shaft. This periosteal arrangement tends to spread along the shaft. The shaft can generally be traced through the tumour, apparently unaffected up to a fairly advanced stage of the disease, and even when the new bone completely surrounds the shaft and very dense masses of bone have formed its continuity can be made out.



## ENDOSTEAL SARCOMA.

*Myeloma.*—The most characteristic feature of this condition in the early stage is the fine trabeculation of the affected area, giving the impression that the tumour is divided up into loculi. This is due to irregularities in the arrangement of the remains of the compact bone surrounding the tumour, and can be well seen in a stereoscopic skiagram. The situation of these tumours at the ends of the bones has been dealt with from the clinical aspect. The X-ray examination confirms this, and also the non-occurrence of extension through the cartilages. The circumscribed and more or less globular expansion of the bone is, of course, a marked feature in the majority of cases. Ultimately the bony shell gets thinned and gives way, and the soft parts then become infected.

## ROUND-CELLED AND SPINDLE-CELLED SARCOMA.

The main feature in this condition is the extreme destruction of bone and the lack of expansion. The shaft above and below the tumour appears absolutely normal right up to the defect.

## DIFFERENTIAL DIAGNOSIS (X-RAY).

Periosteal sarcoma (non-ossifying) may be mistaken for secondary carcinoma of bone, where the primary lesion has evaded notice. There is practically no difficulty in the diagnosis of periosteal sarcoma of the ossifying type. The arrangement of the new bone is typical. I shall show, however, a slide in which a linear fracture of the tibia after an X-ray had been taken was sent to a surgeon as a periosteal sarcoma, but a subsequent skiagram revealed the presence of the fracture.

*Myeloma.*—The differential diagnosis of this condition is extremely difficult, and although the combination of the clinical and X-ray appearances often make it possible, there are a large number of cases in which the X-rays fail to be of any assistance. This is more particularly the case where the diagnosis lies between myeloma and benign cyst.

Bloodgood in his paper on "Giant Cell Sarcoma of Bone," in the August, 1912, number of the *Annals of Surgery*,<sup>1</sup> says, "I would caution against the surgeon making a positive diagnosis of either a bone cyst or a giant cell sarcoma. The more X-rays I see the less confidence have I in my ability to make a differential diagnosis, except in the later stages." This, I think, sums up the situation.

<sup>1</sup> *Annals of Surg.*, Philad., 1912, lxvi, p. 237.

The only points of difference that appear to be of any value are:—

(1) The fusiform expansion of the benign cyst, whereas the myeloma is more globular.

(2) The position in the bone of the benign cyst, not extending to the end of the diaphysis which Mr. Elmslie mentioned in his paper.

(3) Fracture is generally the first symptom that calls for an X-ray examination of benign cyst.

With regard to the differential diagnosis of myelomata by X-rays from inflammatory, specific, or tuberculous lesions, the absence of periost-

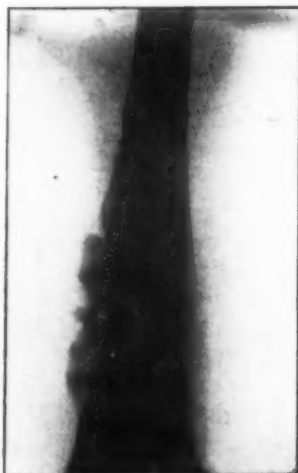


FIG. 1.



FIG. 2.

titis is a valuable sign, but where the diagnosis has to be made from the various cystic lesions the X-ray examination is of very limited value.

Mr. Reid then showed the following slides:—

(a) Fairly early periosteal sarcoma; radiating spicules fairly well seen.

(b) A similar one, with spicules seen on both sides, and the shaft visible through it. (Fig. 1.)

(c) A still more advanced stage; it showed a point at which the periosteum was stripped up, and the whole surrounded by dense bony tissue. (Fig. 2.)

(d) A myeloma of the knee, showing loculation. (Fig. 3.)



FIG. 3.



FIG. 4.



FIG. 5.



FIG. 6.

(e) The same case four years later; the cavity had been filled by bone almost as dense as the surrounding bone.

(f) Myeloid of upper end of fibula, expanding the bone; the bone on the outer side had practically disappeared. The specimen of this was on exhibition.

(g) A very advanced stage of myeloma, showing the bone broken completely through, the upper part being preserved. (Fig. 4.) Specimen shown.

(h) Fracture through a cystic growth of lower end of femur. (Fig. 5.)

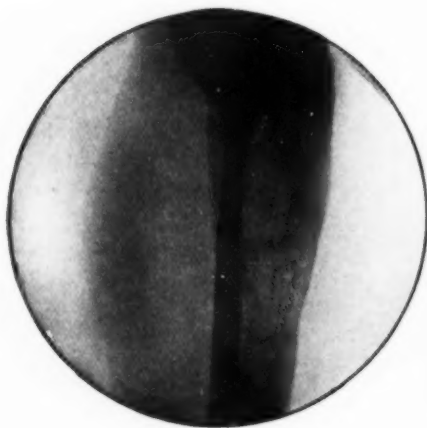


FIG. 7.



FIG. 8.

(i) The same firmly re-united. No operation was done. This was probably a myeloma.

(j) Fracture through what proved to be a myeloid tumour, which might be taken for a cyst. (Fig. 6.) Diagnosed by the microscope.

(k) A case sent up as sarcoma. This was a simple fracture with callus formation. The periosteum shows longitudinal arrangement, so should not have been so diagnosed.

(l) A case similar to that shown by Sir A. Pearce Gould at the last meeting; cystic condition of upper end of humerus. Operation was done, but he had not been able to find the pathological report. Judging by the subsequent history, it was probably innocent.

(m) Showing small layer of specific periostitis.

(n) Case in which malignant disease of spine was suspected; old-standing changes in tibiae were seen, due to osteitis fibrosa. (Fig. 7.)

(o) Secondary carcinoma to show difference from the last.

(p) Cystic condition of bone in shaft of humerus, showing spontaneous fracture. (Fig. 8.) It was opened, and found to contain serous fluid. The lining membrane was taken out and examined microscopically. Mr. Shattock and others pronounced it sarcoma of hæmorrhagic type; large vacuolated cells were visible; 100 mgrm. of radium were inserted next day and left in. Re-union of bone took place very quickly. He had heard recently that the boy remained quite well, and there had been no evidence of extension of disease. He found a case to compare with it in which the X-ray appearances were identical in Dr. Bloodgood's paper in the *Annals of Surgery*, 1910.<sup>1</sup> In Dr. Bloodgood's case the pathological report stated that the lining membrane was formed of connective tissue.

These two cases afforded a good argument against attempting to make a diagnosis by X-ray appearances in such lesions.

Mr. ERNEST SHAW: Primary sarcoma of the long bones occurs mainly in young people, but it also may be met with in older persons. One has briefly to review the variation in position and structure of these tumours; a rough classification has been made dividing them into periosteal and endosteal growths. Microscopically they are found to vary a great deal, and may be divided into round-, spindle-, mixed-celled, and myeloid sarcomas; then we must add the mixed form, which contains cartilage, bone, myxomatous tissue, and calcareous material. With the exception of the true myeloid sarcoma all these tumours are highly malignant, in that they recur after removal, invade surrounding tissues, and reproduce themselves in neighbouring lymphatic glands and distant organs. Although one speaks of periosteal growths in contradistinction to endosteal tumours, it is nearly always found that the former grow into the medulla as well as outwards. They sometimes extend a good distance along the inside of the shaft—a point of importance to remember when considering the scope of operation for their removal. All these tumours occur most commonly at the extremities of long bones, but occasionally the shaft is the primary seat. In the periosteal tumours the cells grow through and incompletely destroy the compact layer of the shaft; on section it is usual to find the remains of the latter running through the tumour and in its normal position.

<sup>1</sup> *Annals of Surg.*, Philad. 1910, lii, pp. 145-83.

This is in marked contrast to what happens in the endosteal variety, for in them the compact tissue is expanded to form a thin layer over the tumour, and the thick shaft ends abruptly at its margin. *Periosteal* sarcomas may be purely cellular—i.e., round-, spindle-, or mixed-celled—or they may be composed of a mixture of these cells and cartilage, bone, or calcareous material. In my experience the mixed variety is the most common. *Endosteal* sarcomas are, in the great majority of cases, myeloid in type—i.e., they contain a large number of multinucleated giant cells, usually lying in small spaces—and a basis of fibrous tissue and spindle cells. They are practically innocent tumours. I have never seen a case which recurred, nor have I seen secondary infection of glands or of other organs. I have been told of one such case, but am very sceptical as to its being a myeloid sarcoma. I find it a common occurrence to see multinucleated cells in small numbers in the periosteal variety of growths, but they must be clearly distinguished from the true myeloid sarcomas, in which giant cells occur abundantly.

The endosteal sarcomas of the shaft, in most of the few cases I have seen, have been of the round- and spindle-celled variety. I can only recall one case of true endosteal sarcoma in the articular end of a long bone which proved to be of the spindle-celled type. In this case an X-ray photograph revealed a tumour in the lower end of the femur of a lady, aged about 50. It was thought that in all probability the growth was a myeloid, and that an amputation through the middle of the thigh would be sufficient. But in order to make quite sure I was asked to cut a section at the time of the operation. The growth proved to be a spindle-celled sarcoma, and so the limb was removed at the hip-joint. This patient died about a year later with secondary growths in the spine and lungs. The practice of having a fresh microscopical section made at the time of operation is one which I consider of great value in these cases, for it is not always possible to make out by ordinary clinical examination that a malignant tumour is present, and I think that every means should be employed to settle the diagnosis before taking off a patient's limb. I know of three cases in which a leg has been amputated for inflammatory swellings due to what is termed "quiet necrosis" of bone.

The spread of sarcoma is usually by way of the blood-stream, and this is easily understood when one considers the intimate relation which exists between the blood-vessels and the tumour cells. It is common to see in sections wide blood-channels only separated from the malignant cells by a layer of endothelial cells. It is not at all uncommon, however,

to see lymphatic glands containing growth; this more often occurs in the purely cellular tumours, but bony growths also spread in this way. The hard bony material found in sarcomas of bone is in the majority of cases a calcareous deposit in the fibrous matrix, not a true imitation of bone trabeculae. In a few tumours well-formed trabeculae do occur. In macerated specimens the gross bony or calcareous tissue is seen in most cases as irregular masses, in a few specimens only is it seen as spicules arranged at right angles to the shaft.

Mr. Shaw added that another point was the difficulty experienced in deciding whether a growth was periosteal or endosteal in origin. In most of the periosteal tumours one found a good deal of growth extending into the cancellous part of the bone, making its way upwards and downwards. In such a case there might be much or little outgrowth into the surrounding tissues. If the case were seen early, there was not much growth on the outside, but a good deal inside the shaft. It might be argued that those growths were endosteal in origin; they might be, but their section differed in appearance from that of real endosteal growths, for in the former one could see the remains of the shaft running through the tumour on each side to its cartilage. In the true endosteal tumour the shaft was always entirely outside the growth, and in many cases expanded. The question of the amount of growth inside these bones was a very important one in view of early diagnosis. If one were to depend on the formation of a visible tumour in a patient's limb, one would not get these tumours very early, because probably the amount of growth inside the bone was much greater than outside. Unfortunately, patients did not seek advice because of such tumours until they noticed a definite lump, or perhaps had some pain in the limb. He did not see how the surgeon could expect to get these cases early, so early as he would? growth were mainly outwards. The X-rays afforded the only means of recognizing the cases early; they enabled one to do at all events the first part of the diagnosis. The final diagnosis must be made by exploratory incision and microscopic examination. Mr. Gask raised the question of the low malignancy of tumours containing cartilage, but he (the speaker) did not think that in those mixed tumours containing cartilage the latter made any difference to the degree of malignancy. But he agreed that where there was a large cauliflower-like mass projecting from the bone, consisting of cartilage on the outside and bone in the middle, the case was not so malignant as the others. But it was not always easy to know whether those tumours were or were not malignant, even from microscopical examination; the



sections might show very few cells, and nearly all cartilage. A few years ago a tumour was put into a London museum and described as one of chondroma of the scapula; it had been removed with part of the scapula. It looked innocent, and when examined microscopically it was pronounced to be innocent; therefore it was labelled chondroma. A year later another specimen was brought from the same case, a recurrence, and accordingly the first specimen had to be re-labelled "chondrosarcoma." A very interesting point was raised at the last meeting by Sir Frederic Eve, and mentioned by Mr. Gask that evening—namely, the registration of these growths. For years he had had it in his mind that all malignant cases ought to be registered, and not only so, but microscopic sections from such cases should be kept in one place, and there was not much question as to where that place should be—namely, the Royal College of Surgeons Museum. He wished the staffs of all hospitals would make a point of seeing that this was done. It was impossible to know too much about such cases as those under discussion, and he hoped the suggestion would be acted upon. If duplicate microscopic sections were preserved in the College Museum, with short note attached, including the name, age, and sex of the patient, they would form an invaluable collection. The accuracy of the diagnosis of all the tumours could be verified, or the reverse, in the light of further knowledge.

MR. CHARLES A. MORTON (Bristol): I should like to speak first about the treatment of myeloid sarcoma. For many years surgeons have recognized that, for this form of sarcoma, the portion of bone in which the tumour is growing may be resected, and that amputation is not required. But up to the year 1898 there was no record of a case of excision of the portion of bone containing the growth from either of the main bones in the lower limb, in this country. At that time I determined to try if I could resect the bone and save the limb even with a myeloid sarcoma occupying the head of the tibia. I resected 3 in. of the upper end of the tibia and  $\frac{1}{3}$  in. from the lower end of the femur, and then screwed the bones together. Although, of course, there is a little more than 3 in. of shortening, yet with the aid of an extra thick sole he has been able to work at a laborious occupation ever since, and has had no recurrence, now fourteen years after the operation. The case is fully reported in the *British Medical Journal* for 1898.<sup>1</sup> In cases in which it may be necessary to excise a greater length of bone than I did in this case, it may be necessary to use a bone-graft to unite

<sup>1</sup> *Brit. Med. Journ.*, 1898, ii. p. 228.

the bones, but I feel sure that, unless the shortening would be very great indeed, it is better to secure firm, bony union between the tibia and femur, by direct union of one bone with the other, and compensate for the shortening by the raised boot.

With regard to what I wish to say with reference to the treatment of periosteal sarcoma, and the forms of central sarcoma other than myeloid, I fear you will not agree with me. We all recognize that periosteal sarcoma is a most deadly disease, and most surgeons believe that the only way to deal with it is by amputation, and some surgeons consider that we must not amputate through the affected bone, even though at a considerable distance from the growth, but always at the joint proximal to it. I suppose we all realize the terrible prognosis of the disease even after amputation. Let me remind you of what Sir Henry Butlin said in the last edition (1900) of his book on the "Surgery of Malignant Disease," based on a very careful study of statistics. He says, writing of periosteal sarcoma of the femur: "Everything leads to the belief that, in the present state of our diagnosis of subperiosteal sarcoma of the femur, amputation of the limb holds out really no prospect of permanent success." We must remember that this was written in 1900, and at a time when we had the aid of radiography in making an early diagnosis. And Sir Henry Butlin also shows that, in two-thirds of the cases of periosteal sarcoma of the leg bones, the patient died with metastases after amputation, though local recurrence was not often present.

In order to show that it is right treatment to excise the portion of bone in which a periosteal sarcoma is growing, and save the limb, surgeons have not to bring forward a series of cases free from recurrence for a large number of years, for no such series can be shown as the result of the sacrifice of the limb. All that is necessary is to show that the results of the adoption of this line of treatment are no worse than after amputation, for it is obviously a great advantage to save the limb. Although in this country there have been very few cases in which a periosteal sarcoma has been excised, yet this has been done in a good many cases by Continental surgeons, and you will remember that when Professor Goldmann came over to this country and spoke at one of our meetings, he told us that he had excised periosteal sarcoma with a result which would have been surprisingly successful after amputation.

But I feel very strongly that in the case of either of the main bones of the lower limbs, it is only if we get the case quite early, when

the growth is only small, that the possibility of resection should be considered, for we must resect a considerable length of what appears healthy bone, above and below the growth, or if it involves the articular end we must take away with it the neighbouring joint, for the growth may extend into its ligaments. I do not wish to take up time by considering the possibilities of bridging a long gap in the tibia or femur by bone-grafting, and this has already been considered at some length by Sir Frederic Eve, but what I wish to emphasize is the need of the removal of a considerable margin of healthy bone with the growth. And when the surgeon has resected the portion of bone on which the tumour is growing I think he should cut it open longitudinally, not only in central sarcoma but even in periosteal sarcoma, to see that he is as far away from the growth in the interior as on the surface, for even a periosteal sarcoma might have advanced farther in the interior of the shaft than was apparent on the surface; and I think all muscles and tendons attached to the affected portion of bone should be cut as far from their attachment as possible.

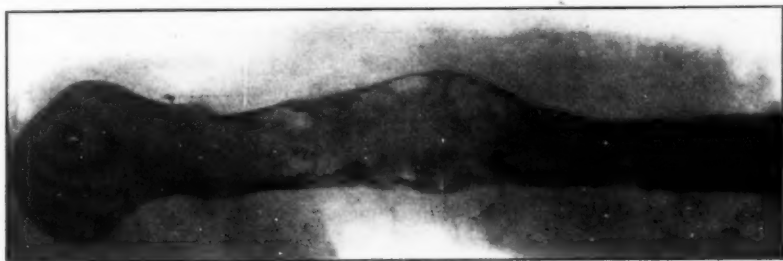
There is one fact which seems to me in favour of reaction in some cases of periosteal sarcoma, and that is that the tumour is very often well differentiated towards the surrounding tissues. Gross, who did such good work in connexion with malignant disease of bone many years ago, found that this was so in almost half the cases of periosteal sarcoma. If, on exploration, I found the growth infiltrating the surrounding muscles, I should regard such a case as unsuitable for excision.

I would venture to point out that surgeons are not always consistent in the practice which they advocate with regard to the treatment of periosteal sarcoma. Sir Henry Butlin has shown ("Operative Surgery of Malignant Disease," 1900 edition) that after excision of a sarcoma of muscle recurrence is almost invariable, and yet excision of such growth has been the accepted practice, and is advised in some of the text-books of surgery rather than amputation of the limb.

In one of my cases I removed the upper half of the fibula for a chondrifying periosteal sarcoma the size of a coco-nut, and the patient had quite a useful limb after the operation. There were two local recurrences; one was excised eight months after the operation, and the other fourteen months after the operation. She had no further local recurrence, but more than three years after the operation she had symptoms of intrathoracic growth from which she died. The full details of the case are published in the *Bristol Medico-Chirurgical Journal* for 1906, vol. xxiv, pp. 313-18.

In the other case I excised the lower end of the tibia, the ankle-joint, and the astragalus, for periosteal sarcoma of the lower end of the tibia. In order to avoid shortening of the leg, I planted the end of the fibula, cut into a joint, into the os calcis, but the result was not satisfactory, and I operated again a year later to replant the foot on the end of the tibia, when I found a recurrent nodule of growth almost the size of a walnut growing from the end of the tibia. I therefore amputated at the knee-joint. The girl, three years after the first operation, had rapidly recurring pleural effusion, due almost certainly to growth in the chest.

You may be inclined to say that the result in both cases justifies the generally received view that in such cases amputation should be performed, and not excision, but I would ask you to remember that the results are no worse than after amputation, and that, in the first case, the patient had good use of the limb for several years before she died from metastatic growth.



Hydatid cyst in the humerus, giving an X-ray appearance like endosteal sarcoma.  
(Skiagram by Mr. C. R. C. Lyster.)

Mr. MURRAY said Mr. Lyster had asked him to speak of a case of which the skiagram was exhibited (*see figure*). It was that of a patient who was sent, three weeks ago, to the Middlesex Hospital on account of swelling of the upper end of the left humerus. It was said to have come on quite suddenly after a slight injury. The skin was red and œdematous, and the condition was thought to be periostitis. The signs of inflammation subsided under treatment, and then he found an enlargement of the humerus which was extremely tender. There was a history of fracture six years previously, and therefore he concluded it must be sarcoma. It was a few days before a bed could be found for her;

in the meantime she had a spontaneous fracture. The skiagram seemed to confirm the diagnosis of sarcoma. They then heard that she had been operated upon at the National Hospital, when a hydatid cyst was removed from the vertebral column. She also had an operation for hydatid cyst of the liver. On making an incision into the swelling for which she came, it was found to be a hydatid cyst. The bone was perforated, and the cyst extended into the soft tissues of the arm.

Dr. IRONSIDE BRUCE: Whilst agreeing with all Mr. Reid has said regarding the radiographic appearances of sarcomata of bone, I would like to show you some skiagrams of what I believe to be typical examples of such tumours, with the object of drawing your attention to the practical value of X-ray examination in the matter of differential diagnosis. My first two skiagrams are examples of endosteal sarcomata, one of the upper end of humerus, and the other involving the head of the radius. In these tumours, the normal uniform dark shadows cast by bone are replaced by shadows which are not uniform, lighter areas, which correspond with the soft parts of the tumour, being seen at irregular intervals. The encroachment of these sarcomata on normal bone produces a characteristic appearance, for no separation or thickening of the periosteum is observable, and where bone has been replaced by the more translucent material of the tumour no abrupt line of demarcation exists. Compact bone being apparently more resistant than cancellous bone, the more translucent material of the tumour is surrounded by the opaque compact bone—an appearance which in my opinion is always present in endosteal sarcoma. The next three skiagrams are examples of periosteal sarcomata of the upper end of humerus, upper end of femur, and lower end of femur. The appearance of these tumours affecting the outer surface of bone differs from that of the former variety, and is in accordance with their more rapid growth and their origin. The bone at the site of the growth is replaced by more translucent material, and appears eroded and irregular in outline. As a whole the affected bone is irregular in structure and diminished in density, and no evidence of periostitis can be detected. The skiagrams at first sight give the impression of want of detail and poor quality, an appearance which is characteristic. When ossification occurs in such tumours, the radiate arrangement of this process is most useful in deciding their nature, and spontaneous fracture when present is a most important observation.

The remaining skiagrams are examples of conditions which, clini-

cally, I believe may be confused with sarcomata, but radiographically are easily recognized :—

- (1) Exostosis of femur.
- (2) Secondary deposit of carcinoma.
- (3) Secondary deposit of carcinoma at a later stage.
- (4) (5) (6) Syphilitic osteitis.
- (7) Typhoidal periostitis.
- (8) Localized osteo-periostitis.
- (9) Central abscess of bone.
- (10) Tuberculous osteitis with central abscess.
- (11) Old ossified scorbutic subperiosteal hæmorrhage.

Mr. S. GILBERT SCOTT: Most of the important points in the diagnosis of these bone tumours have already been dealt with by the previous speakers. In the bone tumours—sarcomata and myelomata—the diagnosis having been made, the question of the degree of malignancy is of vital importance from the point of view of prognosis and treatment. Although myelomata are usually considered slow-growing, they may occasionally be just as rapid in growth and fatal as the true endosteal sarcomata. My impression is that the ratio between the rate of bone *destruction* and *repair*, as is evidenced in the skiagrams, is an important point in determining the probable degree of malignancy in these cases. The more rapid the growth the greater is the destruction and less the repair. A true *endosteal sarcoma* is usually rapid in growth, hence the destruction of bone is rapid—little or no evidence of repair is seen in the skiagrams. On the other hand, a *myeloma* is slower in growth, hence destruction and repair are more evenly balanced. Repair is evidenced by the presence of *bone trabeculæ*. The more marked and dense the shadows of these trabeculæ in the skiagram the slower the growth (fig. 1). One may mention here that these trabeculæ are caused by the varying thickness of the bone-shell. They do not traverse the cavity, as one might be led to suppose from the single skiagram. This can be demonstrated if viewed *stereoscopically*. The more rapid the growth the less marked are these trabeculæ (figs. 2 and 3). If the bone-shell gives way and the disease invades the soft tissues it usually takes on a more rapid growth, although the trabeculæ may for a time remain as well marked as before.

This ratio between destruction and repair is to a certain extent, I think, true of the ossifying *periosteal sarcoma*. Here, however, the rate of repair is estimated from the appearance in the skiagram of the

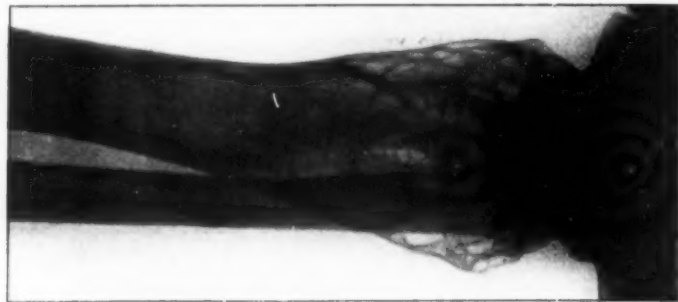


FIG. 1.

Fig. 1: *Myeloma*.—Bone trabeculae well marked; bone expanded; destruction and repair evenly balanced. *Slow growth*.  
Fig. 2: *Myeloma*.—Bone trabeculae not so well marked as in fig. 1; slight expansion of bone; destruction more rapid than repair. *More rapid growth*.

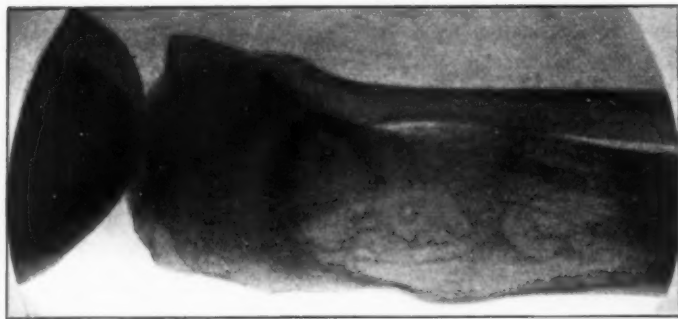


FIG. 2.

Fig. 2: *Myeloma*.—Bone trabeculae not so well marked as in fig. 1; slight expansion of bone; destruction more rapid than repair. *More rapid growth*.



FIG. 3.

Fig. 3: *Myeloma*.—Bone trabeculae absent except at extreme lower part; no bone-shell; rapid destruction with no attempt at repair. *Rapid growth*.



*periosteal striation or spicules*, which, if present, are diagnostic of this disease. These periosteal striations are *at right angles* to the surface of the bone or radial from the tumour and *not parallel* as is seen in *simple periostitis* (figs. 4 and 5). In the next slide, which shows a *lobulated ossifying periosteal sarcoma (local)*, growth has been slow for a time, as is evidenced by the dense new bone. But recently the tumour increased rapidly in size; this has probably taken place in the portion of the



FIG. 5.

FIG. 4.

Fig. 4.—*Periosteal sarcoma*, showing periosteal striations *at right angles* to the surface of the bone at the edge of the growth, practically absent at centre of tumour. *Rapid growth*.

Fig. 5.—*Chronic periostitis (simple)*, showing the periosteal striations *parallel* to the surface of the bone.

tumour where the striations are scanty. These periosteal striations are also seen when a slow-growing myeloma breaks through the bone-shell and invades the surrounding tissues. The so-called *non-ossifying periosteal sarcoma* may only evidence itself in the skiagram by *erosion* of

the surface of the bone and no periosteal striations are seen. These are, I think, the very rapidly growing type, no effort being made at repair. Time makes it impossible to give more than a rough outline of this subject.



FIG. 6.

*Lobulated periosteal sarcoma.*—Tumour localized; the periosteal spicules are very dense and closely packed in upper portion, suggestive of slow growth; more loosely packed in lower portion, suggestive of more rapid growth. In this case a tumour was present for many months and then started to increase in size rapidly.

Dr. HARRISON ORTON said that he was much interested in Dr. Ironside Bruce's last plate, as he himself had a similar case seven years ago, which proved to be one of scurvy rickets. He had not then seen anything quite like it, and so gave a guarded opinion. The question of amputation was considered. Fortunately the child was taken to see Sir Thomas Barlow, who a short time previously had received a book from Germany describing this appearance. The child was then placed on appropriate treatment, and recovered. The shadows were not due to ossification, because in the case he was referring to the shadows cleared up; he concluded it was blood-clot beneath the periosteum. There had been no mention in the discussion of the effect which X-rays had on the sarcoma cells. The question arose whether more could not be done in the treatment of sarcoma by this means, applying the rays after operation. He remembered a case of sarcoma of the parotid, which had recurred several times, and after a few

exposures to X-rays it entirely cleared up. It recurred later in the jaw, but after a few doses of X-rays the tumour again disappeared. The case was shown at the British Medical Association meeting at Leicester as a cure. But twelve months or so after that the growth recurred in the liver. Still, a few applications of the rays caused yet another disappearance; six months later the patient died. The X-rays had a remarkable effect on the growth in this case, although it did not prevent recurrence.

Mr. B. C. MAYBURY sent the following contribution: While endeavouring to trace the after-histories of cases of bone sarcomata admitted to St. Thomas's Hospital during the last eleven years, I found that during this period two patients with myeloid sarcomata had died from secondary growths in the lungs. For this reason I use the term "myeloid sarcoma" in place of the more modern one, "myeloma."

The first case was that of a female, aged 16, who was admitted in August, 1911, with a three months' history of pain in and swelling of the lower part of the right thigh. The symptoms were attributed by the patient to an injury to the knee which she had received some time previously. There was a large, firm swelling attached to the lower end of the right femur on its inner aspect. No pulsation could be detected. There was no egg-shell crackling. Extension of the knee was slightly limited. A note was made to the effect that the skiagram suggested a central bone abscess, but, unfortunately, the plate has not been kept. An exploratory incision was made on September 5, and the tumour was found to consist apparently of blood-clot. A microscopical examination by Dr. Dudgeon, however, showed the growth to be a myeloid sarcoma (see fig. 1). Amputation through the upper third of the thigh was performed on September 12, and the patient was discharged apparently well a fortnight later. Seven months afterwards she was admitted to the North Ormesby Hospital, Middlesbrough, with signs of secondary deposits in the lungs. Death took place in two months, nine months after the amputation. At the post-mortem examination both lungs were found riddled with secondary growths. A portion of the lung was sent to the Yorkshire Pathological Laboratory, and the report of the microscopical examination made by the Director, Mr. Gough, was as follows: "In section the tumour is a mixed-celled sarcoma. Most of the cells are spindles, but some irregular, round and giant forms are found." Unfortunately, I have been unable to obtain a section of the pulmonary growths. A section of the primary growth (fig. 1) was

recently shown to Mr. Shattock, who said that the section was quite typical, and that there was no undue predominance of the irregular-shaped cells that form the background of a myeloid sarcoma.

The second case does not properly belong to this series as the primary growth arose in the os innominatum. The patient, a male, aged 46, was admitted with a seven months' history of right-sided sciatica and dyschezia. *Per rectum* a large fixed mass could be felt projecting from the right side into the pelvis. The pain was so severe that a laminectomy was performed and the posterior roots of all the lumbar and first three sacral nerves divided. The operation, however, gave no relief, and the

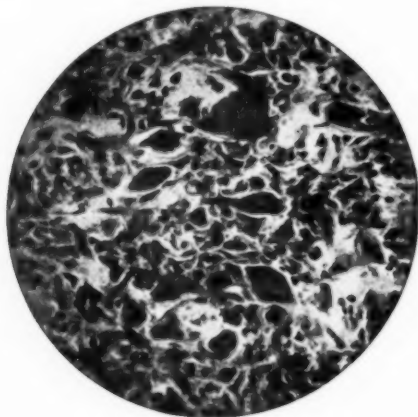


FIG. 1.

Section of myeloid sarcoma of lower end of femur ( $\frac{1}{2}$ ).

patient died a month after admission. A post-mortem examination showed the primary growth to be about the size of a foetal head. It arose from the ilium and grew partly into the pelvis and partly through the obturator foramen into the thigh. Numerous small secondary deposits were found in the lungs. No metastases were discovered elsewhere. A microscopical examination made by Dr. Dudgeon showed both the primary growth (fig. 2) and the pulmonary growth (fig. 3) to be myeloid sarcomata.

The statistics given below, if such a small number is of any value, seem to show that the prognosis in a sarcoma containing cartilage is better than in the other varieties—myeloids, of course, excepted. Taking

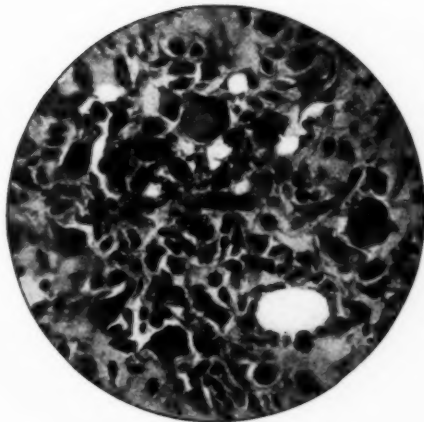


FIG. 2.

Section of myeloid sarcoma of the ilium ( $\frac{1}{6}$ ).

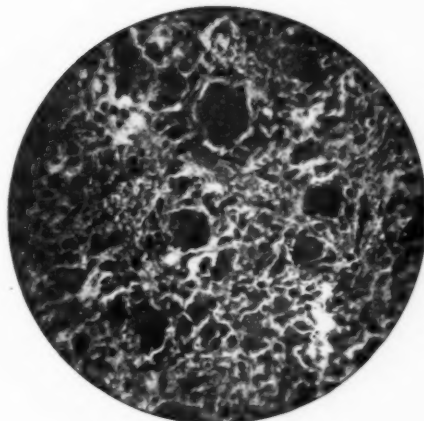


FIG. 3.

Section of pulmonary growth (showing giant cells) secondary to the primary growth shown in fig. 2 ( $\frac{1}{6}$ ). (The photograph is not very clear owing to some degeneration of the growth.)

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only periosteal cases in which a microscopical examination had been made, there were four cases of chondro-sarcomata; one was not traced; of the remaining three, two died two and a half years and five years and nine months respectively after operation; and one was alive two years and seven months later. While of the remaining cases of sarcomata not containing cartilage—fourteen in number—five were not traced; five died within a year, one in fifteen months, one after four years and seven months, and two were alive one year and five months, and one year and eight months respectively after operation.

The only other point I would like to raise is, that unless cases are seen much earlier than at present, a complete ablation of limb—i.e., amputation through the hip- or shoulder-joints or an interscapulo-thoracic amputation—for a sarcoma of the femur or humerus other than a myeloid or a chondro-sarcoma should not be too strongly advocated; and that the question of allowing the patient to retain his limb during the remaining months he has to live be seriously considered. Such patients would be able to continue their work for some time longer until such an accident as a spontaneous fracture occurred. As a general rule, the pain suffered by patients with a periosteal sarcoma is little or *nil*. The results seem to show that it is very doubtful whether an amputation in such cases prolongs life to any great extent. There were eleven cases in which the above amputations had been performed, excluding cases of myeloid sarcomata. Of these, two were not traced; two, both cases of chondro-sarcomata, lived over two years. Of the remaining seven, one was alive one year and eight months after operation; two died, the date of death being unknown, and four died within ten months of the amputation.

# Statistics of Sarcoma of Long Bones from St. Thomas's Hospital (Eleven Years, 1901-1911).

By B. C. MAYBURY, B.S.

|                            |     |     |     |     |     |    |
|----------------------------|-----|-----|-----|-----|-----|----|
| Total number of sarcomata  | ... | ... | ... | ... | ... | 45 |
| Total number of periosteal | ... | ... | ... | ... | ... | 28 |
| " " myeloid                | ... | ... | ... | ... | ... | 17 |

## *Periosteal.*

|                      |     |     |     |     |     |    |
|----------------------|-----|-----|-----|-----|-----|----|
| Not traced           | ... | ... | ... | ... | ... | 11 |
| Died within 6 months | ... | ... | ... | ... | ... | 4  |
| " " 1 year           | ... | ... | ... | ... | ... | 3  |
| " " 2 years          | ... | ... | ... | ... | ... | 1  |
| " " 3 "              | ... | ... | ... | ... | ... | 1  |
| " " 4 "              | ... | ... | ... | ... | ... | 0  |
| " " 5 "              | ... | ... | ... | ... | ... | 1  |
| " " 6 "              | ... | ... | ... | ... | ... | 1  |
| " date unknown       | ... | ... | ... | ... | ... | 3  |
| Well over 6 months   | ... | ... | ... | ... | ... | 0  |
| " " 1 year           | ... | ... | ... | ... | ... | 2  |
| " " 2 years          | ... | ... | ... | ... | ... | 1  |
| " " 3 "              | ... | ... | ... | ... | ... | 0  |
| Total                | ... | ... | ... | ... | ... | 28 |

## *Myeloid.*

|                      |     |     |     |     |     |    |
|----------------------|-----|-----|-----|-----|-----|----|
| Not traced           | ... | ... | ... | ... | ... | 8  |
| Died within 6 months | ... | ... | ... | ... | ... | 1  |
| " " 1 year           | ... | ... | ... | ... | ... | 1  |
| Well over 6 months   | ... | ... | ... | ... | ... | 0  |
| " " 1 year           | ... | ... | ... | ... | ... | 1* |
| " " 2 years          | ... | ... | ... | ... | ... | 0  |
| " " 3 "              | ... | ... | ... | ... | ... | 2† |
| " " 4 "              | ... | ... | ... | ... | ... | 0  |
| " " 5 "              | ... | ... | ... | ... | ... | 0  |
| " " 6 "              | ... | ... | ... | ... | ... | 1  |
| " " 7 "              | ... | ... | ... | ... | ... | 1  |
| " " 8 "              | ... | ... | ... | ... | ... | 0  |
| " " 9 "              | ... | ... | ... | ... | ... | 1  |
| " " 10 "             | ... | ... | ... | ... | ... | 1  |
| Total                | ... | ... | ... | ... | ... | 17 |

\* No operation; condition unchanged.

† One case; no operation; condition unchanged.



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PERIOSTEAL SARCOMATA.

| Case | Sex   | Age | Bone | Position | Duration             | Operation | Histological examination                                  | Result, with remarks                                       |
|------|-------|-----|------|----------|----------------------|-----------|---|--|
| 1    | A. S. | M.  | 41   | Femur    | Upper end            | 10 weeks  | None  | Not traced; (?) case of sarcoma                            |
| 2    | W. S. | M.  | 55   | Tibia    | Head                 | 6 months  | None (inoperable)   | Died in 6 months; iliac glands; (?) endosteal growth       |
| 3    | T. S. | M.  | 59   | Femur    | Shaft, $\frac{1}{3}$ | 4 months  | None  | Not traced   |
| 6    | H. W. | M.  | 21   | Ulna     | Upper end            | 13 months | Amputation of upper arm, $\frac{3}{4}$                    | Recurrence in stump 1 month after operation                |
| 7    | W. S. | M.  | 3    | Femur    | ?                    | 7 months  | Re-amputation at shoulder-joint                           | Died 4 months after first operation with secondary growth  |
| 8    | G. W. | M.  | 26   | Clavicle | ?                    | 15 months | Amputation at hip-joint                                   | Not known; (?) case of sarcoma                             |
| 9    | G. Y. | F.  | 3    | Tibia    | Shaft, middle third  | 5 weeks   | Excision of recurring growth                              | Not known; first operation elsewhere, 9 months ago (?)     |
| 14   | A. N. | F.  | 13   | Femur    | Lower end            | 6 months  | Amputation of thigh (supra-condylar)                      | Not traced   |
| 16   | A. J. | F.  | 24   | Tibia    | Shaft, upper third   | 7 months  | Amputation of thigh, $\frac{4}{5}$                        | Died $5\frac{1}{2}$ years after operation                  |
| 18   | A. B. | M.  | 14   | Humerus  | Shaft, whole length  | 1 month   | Amputation at shoulder-joint                              | Not traced   |
| 19   | J. K. | M.  | 33   | Femur    | Shaft, middle third  | 6 months  | Re-amputation inter-scapular thoracic                     | Recurrence in stump 6 weeks after operation                |
| 21   | M. L. | F.  | 14   | Fibula   | Shaft, lower third   | 18 months | Amputation of thigh, ? site                               | Not traced   |
| 23   | S. M. | M.  | 62   | Humerus  | Shaft, middle third  | 14 months | Amputation of leg (seat of election) + excision of fibula | Recurrence in skull 4 years 4 months after first operation |
| 25   | W. G. | M.  | 13   | Radius   | Shaft, lower third   | 4 months  | Cerebral decompression                                    | Died 4 years 7 months after first operation                |
|      |       |     |      |          |                      |           | Amputation at shoulder-joint                              | Died, date unknown; (?) endosteal                          |
|      |       |     |      |          |                      |           | Amputation of upper arm, middle third                     | Not traced   |

|    |         |    |     |         |                     |             |   |                                |  |
|----|---------|----|-----|---------|---------------------|-------------|---|--------------------------------|--|
| 27 | B. F.   | F. | 14  | Femur   | Lower end           | 3 months    | None (general dissemination)                              | None                           | Died 6 weeks after discharge   |
| 28 | V. B.   | M. | 18  | Femur   | Shaft, lower third  | 2 months    | Amputation at hip-joint                                   | Chondro-sarcoma                | Died 2½ years after operation  |
| 29 | F. P.   | F. | 15  | Tibia   | Upper end           | 2 months    | Amputation of thigh, $\frac{3}{4}$                        | Spindle-celled                 | Died 15 months after operation   |
| 30 | C. S.   | F. | 58  | Humerus | Head                | 13 months   | Interscapulo-thoracic                                     | Mixed-celled                   | Died 10 months after operation   |
| 31 | P. McD. | M. | 10  | Humerus | Upper end           | 1 week      | No radical operation                                      | (Mr. Shattock)<br>Round-celled | Recurrence in orbit 5 months after first admission; died 11 months after first admission |
| 32 | K. W.   | F. | 31  | Femur   | Shaft, upper third  | 2 years (?) | Amputation at hip-joint                                   | Round-celled                   | Died 4 months after first operation with secondary growths                               |
| 34 | F. W.   | M. | 32  | Fibula  | Shaft, middle third | 12 months   | Amputation of leg (seat of election) + excision of fibula | None                           | Not traced   |
| 36 | F. M.   | M. | 19  | Femur   | ?                   | ?           | None (inoperable)   | None                           | Not traced   |
| 37 | C. J.   | M. | 32  | Humerus | Upper end           | 9 months    | Interscapular thoracic                                    | Spindle-celled                 | Died, date unknown   |
| 38 | E. C.   | F. | 18  | Humerus | Shaft, upper third  | 6 weeks     | Amputation through shoulder-joint                         | Chondro-sarcoma                | Well 2 years 7 months after operation  |
| 39 | G. D.   | M. | 17  | Humerus | Shaft, upper third  | 12 weeks    | Amputation through shoulder-joint                         | Spindle-celled                 | Died 9 months after operation  |
| 41 | B. E.   | M. | 21  | Fibula  | Shaft, upper third  | 9 months    | Amputation of thigh (supra-condylar)                      | Spindle-celled                 | Well 1 year 5 months after operation   |
| 44 | T. T.   | M. | 38  | Femur   | Lower end           | 3 months    | Amputation of thigh, $\frac{2}{3}$                        | Spindle-celled                 | Died, date unknown   |
| 45 | A. D.   | M. | 10½ | Femur   | Lower end shaft     | 3 months    | Amputation at hip-joint                                   | Spindle-celled                 | Well 1 year 8 months after operation   |

## MYELOID.

|   |       |    |    |       |           |          |                                    |                 |            |
|---|-------|----|----|-------|-----------|----------|------------------------------------|-----------------|------------|
| 4 | W. L. | M. | 34 | Femur | Lower end | 5 years  | Amputation of thigh, $\frac{3}{4}$ | Myeloid sarcoma | Not traced |
| 5 | A. G. | M. | 26 | Femur | Lower end | 2 months | Amputation of thigh                | Myeloid         | Not traced |

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MYELOID—(continued.)

| Case     | Sex | Age | Bone    | Position  | Duration               | Operation  | Histological examination                     | Result, with remarks  |
|----------|-----|-----|---------|-----------|------------------------|--|--|---|
| 10 M. E. | F.  | 27  | Tibia   | Head      | 1 year                 | Amputation of thigh, $\frac{2}{3}$ / $\frac{1}{3}$               | None   | Not traced; "endosteal" (?) myeloid   |
| 11 W. B. | M.  | 31  | Femur   | Lower end | 7 weeks                | Amputation of thigh, $\frac{2}{3}$ / $\frac{1}{3}$               | None (specimen to Royal College of Surgeons) | Well 10 years after operation   |
| 12 L. M. | F.  | 28  | Femur   | Lower end | 16 months              | Amputation of thigh, middle third                                | Giant - celled sarcoma                       | Not traced  |
| 13 H. G. | F.  | 18  | Femur   | Lower end | 1 month                | None   | None   | Not traced; (?) myeloid   |
| 15 J. O. | M.  | 26  | Femur   | Lower end | 5 months               | Amputation of thigh, middle third                                | Giant - celled                               | Well 9 years after operation  |
| 17 R. T. | M.  | 49  | Radius  | Lower end | 2 years                | Excision of lower half of radius + insertion of aluminium radius | Giant - celled                               | Died 3 weeks after operation with cellulitis and pericarditis                       |
| 20 L. C. | F.  | 27  | Femur   | Lower end | 5 months               | Amputation of thigh, $\frac{2}{3}$ / $\frac{1}{3}$               | Giant - celled                               | Well $7\frac{1}{4}$ years after operation   |
| 22 D. W. | F.  | 5   | Fibula  | Upper end | 10 months              | Excision of upper third of fibula                                | Giant - celled                               | Not traced  |
| 24 J. M. | M.  | 30  | Femur   | Lower end | 2 years                | Amputation of thigh, middle third                                | Giant - celled                               | Not traced  |
| 26 W. B. | F.  | 12  | Tibia   | Head      | 6 months               | Amputation of thigh, lower third                                 | Myeloid                                      | Well 6 years after operation  |
| 33 A. L. | M.  | 28  | Femur   | Upper end | 22 months              | None (inoperable)  | None   | Well 3 years after discharge; (?) myeloid   |
| 35 F. F. | M.  | 30  | Femur   | Lower end | 12 months              | Amputation of thigh, middle third                                | Myeloid                                      | Well $3\frac{1}{2}$ years after operation   |
| 40 E. C. | F.  | 21  | Femur   | Upper end | 3 years                | None   | None   | <i>In statu quo</i> 13 months later; (?) myeloid                                    |
| 42 M. Q. | F.  | 16  | Humerus | Head      | 8 $\frac{1}{2}$ months | Interscapulo-thoracic  | Giant - celled                               | Not traced  |
| 43 W. B. | F.  | 16  | Femur   | Lower end | 3 months               | Amputation of thigh, $\frac{1}{2}$ / $\frac{1}{3}$               | Giant - celled                               | Signs of secondary nodules in lungs; operation, 1912; died 9 months after operation |

The PRESIDENT (Mr. G. H. Makins, C.B.) said his first duty was to thank Sir Alfred Pearce Gould, Sir John Bland-Sutton, Sir Frederic Eve, Mr. Gask, Mr. Reid and others who had contributed opening addresses in the discussion; also the several authorities at the Hospital Museums, who had allowed the fine series of specimens to be exhibited on loan. The meeting would also wish to thank Mr. Maybury for kindly preparing a similar set of cases from St. Thomas's Hospital to those which Mr. Gask had compiled from St. Bartholomew's Hospital, although, unfortunately, there had not been time to allow Mr. Maybury to deal with them. He thought the Section could congratulate itself on the discussion having been a success. Though it had been suggested that it would be simply an educational discussion, a number of important points had been brought out. Sir John Bland-Sutton raised the suggestion that a number of so-called simple bone cysts might have had their origin in myeloid sarcoma. A specimen of myeloid sarcoma of the fibula on the table, already a multilocular cyst, showed a step in this direction.<sup>1</sup> Sir Frederic Eve had spoken in a damaging sense of the myeloid sarcomata, though he brought forward no fresh cases to substantiate his position. Among the cases at St. Thomas's Hospital which had been collected by Mr. Maybury, there were two of interest in this particular, one an apparently undoubted myeloid sarcoma of the femur, in which the patient died nine months afterwards with secondary growths in the lung. The histological specimen of the original tumour in this case was available, and had been seen by Mr. Shattock and other competent pathologists. Mr. Shattock had expressed the opinion that it must be regarded as typical myeloid sarcoma. The patient died in the country, and a histological specimen, which had been prepared, could not be obtained; the pathologist's report was to the effect that it was a "mixed sarcoma." During the same period another case occurred which could not properly be included in this table of tumours of the long bones, one of myeloid sarcoma of the pelvis; that patient also died with secondary growths in the lungs, and histological specimens from both primary and secondary growths in the case were in the room. An important point arising out of these observations was as to the expediency of giving up the old term "myeloid sarcoma," and speaking of these tumours as myelomata, since the latter term might permit of some misunderstanding. It was more reasonable to regard these

<sup>1</sup> St. Thomas's Hospital Museum, No. 665a.

tumours as related to the sarcomata than to put them into the same category as the multiple myelomata, with which they had little in common. It was not difficult to understand a patient with myeloid sarcoma getting secondary growth. In any slowly progressing case of sarcoma secondary growths might eventually appear rapidly. A patient present in the room afforded an interesting example of that fact. After an injury to the hand a swelling of the metacarpal bone developed which on removal was said to be composed of fibrous tissue, the result of inflammatory change. A tumour then developed in the soft parts near the shoulder, which proved to be a typical fibro-sarcoma. The second tumour was removed only three months ago, and now there was a third secondary growth in the scapula, and a skiagram showed a fourth starting in the great trochanter of the femur. The growths now rapidly developing were obviously of more malignant type than the original tumour. In looking over a number of histological specimens of myeloid sarcomata the structure of the base tissue was found to vary very much in appearance, in some cases closely resembling the malignant varieties. One point had not been mentioned of which there was an interesting example among the specimens exhibited—namely, the question whether sarcoma ever developed upon a recent fracture.<sup>1</sup> The subject of this tumour was in St. Thomas's Hospital, under Mr. Mackellar. The humerus was fractured about its centre and united. Six weeks afterwards a swelling formed which was thought to be superabundant callus. Four and a half months later the arm was amputated on account of rapid increase in the size of the tumour, which was found to be a chondro-sarcoma of the humerus. The specimen suggested that fracture was the primary event, since the shaft of the bone had undergone little change, and that the growth had developed around the seat of the fracture. That was a practical point which often exercised the mind of the surgeon, and it was a pity that there had not been time for more attention to be paid to it. Sir Frederic Eve said the fear of cutting into a sarcoma was probably overrated, but his (the speaker's) experience did not lead him to agree with the statement. If he had to cut into sarcoma for histological purposes, he made preparations to do amputation within the ensuing twenty-four hours. In the case of one of the specimens on the table,<sup>2</sup> the patient came to the hospital with a swelling in

<sup>1</sup> St. Thomas's Hospital Museum, No. 625a.

<sup>2</sup> St. Thomas's Hospital Museum, No. 628.

the lower end of the radius. Being uncertain of its nature, the surgeon made an incision, and finding solid bone concluded it was a case of osteitis. At the time of the exploration the tumour was very small, but during the ensuing two months a large number of secondary growths developed in the glands, soft tissues of the limb, the lungs and pleura, obviously of the same character, and caused the death of the patient. The speaker had never seen a case in which secondary growths occurred so rapidly, and probably the incision was responsible for this occurrence. The remarks made by Dr. Elmslie and Mr. Shaw as to the necessity of going to the bottom of the sarcoma when getting a histological specimen were important; a piece taken from the surface was, in many cases, absolutely valueless, and the opinion expressed on it misleading. With regard to the diagnosis of myeloid sarcoma, there was a macerated specimen from St. Thomas's Museum of a round-celled sarcoma of the femur, of rapid growth;<sup>1</sup> which anyone might say was a skeleton of a myeloid sarcoma. It was not only a fairly complete skeleton, but it possessed the ordinary rounded form of a myeloid sarcoma at the end of a bone; and it seemed of importance as showing that one could not always judge by the arrangement of bone and the shape of the tumour that one was dealing with myeloid sarcoma. A skiagram of a tibia was exhibited showing the same conditions; the tumour in this case proved to be spindle-celled sarcoma, possibly a periosteal one invading the bone, but from the skiagram the uninitiated surgeon would say it was myeloid sarcoma. The X-ray picture did not always enable one to make a certain diagnosis. With regard to prognosis in the periosteal sarcomata, not much hope was to be gleaned from the discussion. The removal of the entire bone in periosteal sarcoma was one of the earliest instances of an attempt to do a radical operation for malignant disease. It had been an absolute failure, and whatever opinion might be entertained as to the proper course to follow it was impossible not to sympathize with the proposition that it is not always advisable to be thoroughly radical in these cases. It was a painful task to the surgeon to undertake high amputations for this disease, the only object of which was to prevent unnecessary suffering from spontaneous fracture, or some other complication. If cases could be treated in a less drastic manner with an equal degree of success, poor as the results might be, it would prove of some satisfaction both to the surgeon and the patient.

<sup>1</sup> St. Thomas's Hospital Museum, Nos. 640 and 641.

[A series of over 100 specimens of sarcomata and myelomata of long bones, kindly lent by various metropolitan museums (Guy's, Middlesex, Royal Free, St. Bartholomew's, St. Mary's, St. Thomas's and Westminster) and numerous lantern slides and skiagrams by Mr. Reid, Mr. Scott, Dr. Orton, Mr. Hey Groves and others, were exhibited at both meetings and during the intervening week.]



## **Surgical Section.**

December 10, 1912.

Mr. G. H. MAKINS, C.B., President of the Section, in the Chair.

### **The Results of Filigree Implantation.**

By LAWRIE MCGAVIN, F.R.C.S.

ALTHOUGH eight years have passed since the method of implanting filigree of silver wire was devised by Bartlett for the cure of abdominal hernia, and although much has been written regarding the saccular theory of the origin of inguinal and femoral hernia, and other matters concerning these conditions, surgeons seem to have had little to tell the profession with regard to the ultimate results of operations, whether applied by Bartlett's method to ventral or by my own double-filigree operation to inguinal hernia. Whether this is due to diffidence in submitting patients to what may at first sight appear to be a drastic method, or to lack of sufficient material for publication, the fact seems to me regrettable.

Of the large number of hernias operated upon in these years, there must be many which have been treated by filigree implantation, since I know of several surgeons who, like myself, have been most favourably impressed by this method and have frequently employed it. Owing, however, to lack of published results, I have been compelled to fall back upon my own work from which to draw practical conclusions, and although as a consequence the number of my cases is necessarily small (since I have never employed nor advocated filigree implantation as a routine method), I can vouch for these cases having been of such a character as to preclude the probability of their cure by any means other than that which I am dealing with. It is with a view to inducing the profession to consider the advisability of abandoning the out-of-date truss or belt for more modern methods that I have ventured to put before this Society the results I have obtained by a method which I believe constitutes a marked advance in the surgery of abdominal and inguinal hernia.

I think it will be generally admitted, firstly, that in really suitable cases Bassini's operation for inguinal hernia is an excellent method, and in most young adults with only moderate protrusions will, when properly applied in chosen cases, result in a cure. Secondly, that when recurrence takes place, a cure by this method is highly problematical. Thirdly, that in the event of failure, such further attempt, by increasing the amount of stretchable cicatrix, distinctly increases the prospect of recurrence. Fourthly, that the ultimate application of a truss is a confession of failure, a disappointment to the patient, and in many cases, from its continuous pressure, a factor in the final enlargement of the hernial gap. Lastly, that ventral hernias in the stout and elderly are in the majority of cases uncontrollable by any form of apparatus, owing to the failure of such superficial pressure to prevent the lateral spread of the hernia in the deeper planes of the thick abdominal wall, the constant

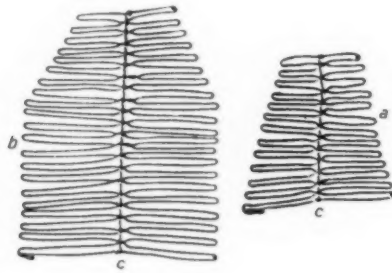


FIG. 1.

a, Pubic section; b, iliac section; c, midrib of filigree.

increase of the extraperitoneal fat, and the progressive distension of the abdomen common to such patients.

It was with these ideas that I turned to filigree implantation as a method promising more to surgeons and patients than the older operations. I may say that my expectations have been very fully confirmed. I have found the method simple, safe, and sound in practice, and at the present moment no patient on whom I have operated has been or is wearing a truss, belt, or support of any kind.

My cases of hernia of all varieties, excepting femoral hernia, done since the introduction of filigree implantation number 314. Of these 263 were inguinal and 51 were umbilical or ventral. Of the inguinal cases, 106 were treated by filigree implantation, and of the umbilico-ventral 40; adding to these 20 cases of inguinal implantations done on both sides, the total number of implantations of all varieties is 166.

This, it is true, is not a very large number, but it is probably as great as can be shown at present by any one surgeon, not using the method as a routine practice, and it is sufficient from which to draw conclusions when it is remembered that careful note has been kept of the after-history of most of the cases, and in view of the fact that several years have passed since the method was first employed.

As regards the sex and age of the patients, the conclusions are, I think, especially valuable, since in the case of the inguinal hernias all but six were men, and my work lying especially among seamen, many of them were engaged in the hardest of all manual labour—viz., stoking. In the case of the fifty-one umbilical and ventral hernias, again, only fifteen were men and thirty-six women, many of these latter being

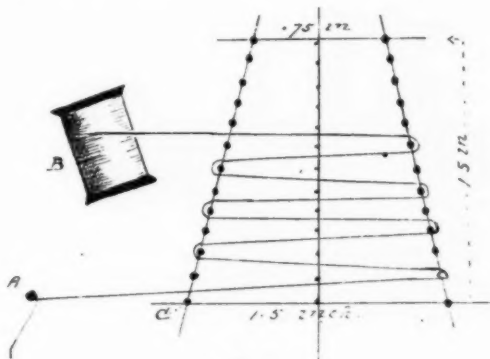


FIG. 2.

Method of making the sections. *A*, anchor pin; *B*, bobbin; thirteen pins on either side; *C*, point at which loose ends are twisted on completion of zigzags; the black dots represent pins.

enormously stout. Some of both sexes had undergone repeated operations ineffectually, and many had been refused operation more than once as being quite incurable. It is clear, therefore, that if these patients are to-day in a fit state to carry on their work and enjoy life free from the encumbrance of trusses, belts, and binders, and I know not what else, the operative treatment which I have striven to popularize must be considered to be a very great advance on the older methods.

As advanced age has usually been considered a contra-indication to operation, since the latter has so often been followed by recurrence in these cases, I am pleased to find that of the 146 cases of implantation eleven were over the age of 60, the two oldest being 72 and 67;

twenty-seven were between the ages of 50 and 60, while forty-eight were between the ages of 40 and 50, the remainder being under the age of 40. Thus eighty-six cases were beyond the age at which we usually consider the prospect of cure problematical, and yet with the two exceptions to be mentioned presently none of them has shown any sign of recurrence. The impossibility of effecting a radical cure in hernias of great size by any of the ordinary methods of approximation is, of course, well known; when such has been attempted by the operations of Bassini, Kocher, Halsted, and other masters of surgery, the result has been in nearly all cases, whether assisted by a truss or not, early recurrence, rendering the ultimate cure by more modern methods doubly difficult. The cases which form the basis of this paper were dealt with by implantation for one or more of the following reasons: they were either of large size, long standing, in elderly subjects, affected

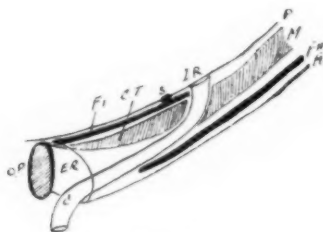


FIG. 3.

Horizontal section of inguinal canal, showing correct position of filigrees. A, aponeurosis; C T, conjoined tendon; C, spermatic cord; O P, symphysis pubis; F', pubic section of filigree; F'', iliac section of filigree; E R and I R, external and internal rings; S, neck of sac tied off; P, parietal peritoneum; M, muscle.

by the atrophy of truss pressure, exhibited a wide hernial gap, or occurred in men whose work was unusually heavy. The test has therefore been a practical one in every respect.

That some of these hernias have been of vast dimensions the slides I propose to exhibit to you presently will demonstrate: they have required patience, hard work, and the facing of considerable risk to cure, and the fact that most of the patients are to-day well and strong is a high testimonial to the efficacy of the method of implantation.

Experience has, however, taught me that certain conditions must be fulfilled if recurrence is to be avoided. In all these cases there have been two recurrences, both were cases of inguinal hernia. Now it is

well known that in ordinary cases recurrence is almost always the result of sepsis or faulty technique. In filigree cases it *may*, but rarely *does*, follow sepsis, and is more likely to follow faulty technique; but excluding these causes, recurrence even in the worst of filigree cases is so far unknown.

With regard to my recurrences, the first was one of my earliest cases of inguinal hernia; it was already a case of recurrence. Suppuration unfortunately occurred after implantation and the iliac section (fig. 1, *b*) shifted its position. I waited till the resulting sinus had healed, and I then repeated the operation, implanting a fresh iliac section. The wound healed by primary union, and the patient is now, after six years, sound and well. The second case was due to faulty technique on my own part. Trusting to the intra-abdominal pressure for support, I placed

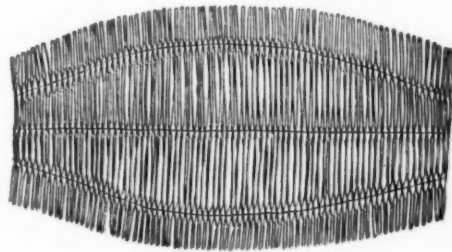


FIG. 4.

Pattern of abdominal filigree used by the author; extreme width 5 in., length varying from 6 in. to 10 in.

the pubic section (fig. 1, *a*) of the filigree upon extraperitoneal tissue which proved too loose and lax to hold it in position, with the result that it shifted outwards about an inch, the hernia recurring a year later between the filigree and the pubic spine. The operation was therefore again performed, a fresh pubic section was placed upon the conjoined tendon instead of beneath it, the old pubic section being retained in position. This case has only recently been done. There is no other case of recurrence in my series, although many of them have been done for more than six years. I may mention here that the spontaneous shifting of an abdominal filigree is impossible, and in one or two cases of persistent sinus after implantation in which the filigree appeared to have shifted the trouble has been due to the ill-advised use of probes and sinus forceps. On the only two occasions on which I have had to

remove any portion of a filigree the reason was displacement of wires into the sinus from this cause. A filigree implanted and resulting in a primary union is, after a short time, so absolutely incorporated with the tissues that it can only be removed by excision "*en bloc*," or by extraction of its wires one by one. The only effect of suppuration in the case of abdominal filigrees has been to fix them even more firmly than in the case of primary union.

The presence of these filigrees has given rise to no untoward symptom: there has been no case of pain, discomfort, swelling, or atrophy of the testis; nor has there been any evidence in the few autopsies of which I have knowledge of the excessive formation of adhesions, even below the level of the semilunar fold of Douglas, where an abdominal filigree has rested actually upon the peritoneum. As showing the efficacy of this method, I operated some time ago on a naval officer for a large ventral hernia following appendicectomy, implanting an 8-in. filigree. After convalescence he was engaged in hard and rough work, and when I saw him again this year a skiagram showed his filigree to be broken in one or two places; in spite of this his abdominal wall is sound and strong, and he wears no support whatever.

I have once been met with the necessity of operating upon the abdomen of a patient in whom I had already implanted a 7-in. filigree. I found no difficulty in approaching the abdominal cavity by an incision along the right margin of the rectus, and was able without disturbing the filigree to remove a tumour weighing 25 lb.

Some years ago a patient wrote and told me that his wound (an inguinal implantation four years old) had opened and that the filigree was coming out. I did not believe such a thing to be possible, silver wire being non-absorbent and antiseptic, I therefore took the trouble to find out the particulars, and discovered that he had had an attack of gonorrhœa with a large bubo which had broken down and laid bare the iliac section of his filigree. Ultimately the scar healed and he has remained perfectly well.

The difficulty and danger of dealing with some cases of ventral and inguinal hernia depend largely on the size of the mass and the extent of the adhesions present. Two cases will illustrate this: A girl, aged 23, was sent to me some years ago through the kindness of Sir Alfred Fripp and Mr. Arbuthnot Lane. She had developed a very bad ventral hernia following an operation for appendicular abscess and general peritonitis, with the subsequent formation of a fæcal fistula. Six operations were performed for this latter, and subsequently several attempts were made

without success to close the large hernial gap which resulted. At the operation (I believe it was her ninth) it took me an hour to free the adherent coils of intestine from each other and from the cicatrix, and I then found the peritoneum so destroyed that I could not close the abdomen; a gap of 3 in. by  $1\frac{1}{2}$  in. was left in the peritoneum. I was ultimately compelled to suture the ileum to the cæcum, and these two to the margins of the gap, in order to make a bed on which to lay the filigree. No difficulty arose subsequently, and since that time she has married and borne children without any return of the hernia. The second case was that of a married woman, aged 62, with an umbilical hernia measuring 33 in. in circumference (fig. 5) and containing 10 ft. of small intestine, the whole of the omentum, the sigmoid, and part of

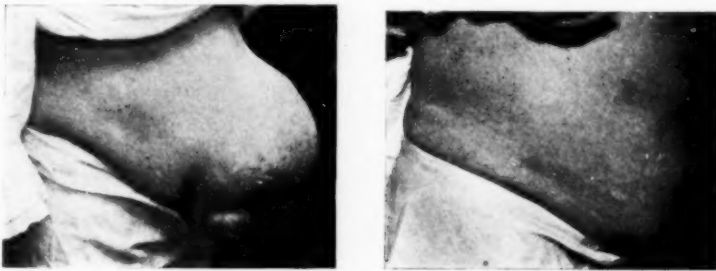


FIG. 5.

Lateral view showing extent of forward protrusion and sacculation below navel.

Front view after operation, showing reduction in size of abdomen and length of incision; 9-in. filigree implanted.

the transverse colon. She was submitted to operation in the Dreadnought Hospital six years ago. The difficulty of closing the abdomen was so great that three pairs of hands were required to accomplish the reduction, and the operation lasted three hours. This patient is, however, to-day doing her work as cook in a military mess, and is well and strong and wearing no support of any kind. Many of my cases have been of this nature.

It might be supposed that any severe stretching of the abdominal wall shortly after operation might tend to undo the work done. This, however, is not so. The case I have mentioned of the patient from whom I removed a 25-lb. tumour is proof of this fact. A second case in support is to be found in that of a patient for whom I implanted an 8-in. filigree during the fifth month of pregnancy as an alternative to the



induction of abortion, which had been previously twice performed. She went to term after operation, was normally confined, and is in perfect health to-day. A third patient has borne two children within twenty months of her implantation, and in spite of the size of the filigree (9 in. in length) there is not the slightest sign of return of the hernia (fig. 6).

I have found hernia following appendicular abscess particularly troublesome to deal with, owing not only to the extensive adhesions, as already stated, but to the difficulty of covering the filigree with anything except skin and superficial fascia, the rectus muscle often refusing to be brought into apposition with the internal oblique and transversalis muscles. A wide gap is thus often left, in which blood, serum, and clot



FIG. 6.

Front and lateral views of hernia, showing extensive sacculation requiring very wide excision; 9-in. filigree implanted.

collect, rendering a primary union very difficult to secure. Such a case, in a very stout woman, came under my care last year, a gap 1 in. wide and 4 in. long remaining at the end of the operation between the filigree and the integuments. This accumulation had to be evacuated at the end of ten days, but no suppuration took place, and the sinus healed at the end of three weeks, the patient being sound and well at the present time.

Suppuration is, of course, more frequently seen than in straightforward cases, whether inguinal or ventral, since the enormous size of these hernias, the unhealthy condition of the patients, the great amount of the manipulation, and the consequent serous oozing, make it more than usually difficult to secure asepsis. I find that of the cases of all types of ventral hernia treated by implantation—viz., fifty-one—

three suppurated badly, and one slightly; all four did well, and have sound abdominal walls to-day. Of the inguinal cases treated by implantation—viz., 126—two suppurated slightly and one badly. In two the filigree shifted, and the operation was again performed, and in one no shifting took place. All of these cases are well to-day, and have been for the last three years. In two cases out of four strangulated inguinal hernias filigrees were implanted. The first was the case of a man, aged 64, with a severe strangulation of 14 in. of ileum; in the second the patient was aged 54, and the strangulation involved 8 in. of ileum and was recent. No infection of the filigrees took place, and the patients remain sound and well.

It is not to be expected, in dealing with such huge hernias, that the mortality will be that of ordinary cases. The risks are greater, since the subjects are less healthy, and the interference with tissue greatly increased. Thus among the forty ventral cases there were four deaths (10 per cent.): one from broncho-pneumonia, one from pulmonary embolism, one from cardiac failure, and one from ileus. All were in very stout patients, and all with one exception had very large hernias. This latter had three weeks previously undergone implantation for a gigantic inguino-scrotal hernia quite successfully, but failed to rally after the same operation for a comparatively small umbilical rupture, his death occurring from ileus.

Among the inguinal cases there was only one death (0.9 per cent.), which was due to ileus. The patient was enormously stout, with a hernia measuring 32 in. in circumference. This case was only done at the urgent request of the patient, who really realized the very grave risk he was incurring.

The short time at my disposal does not permit of my going more fully into detail on the subject of filigree implantation, and I will therefore state simply the conclusions which have been forced upon me by the work I have done:—

- (1) Few, if any, hernias, whether inguinal or ventral, can now be considered incurable.
- (2) In filigree implantation is to be found the only true radical cure that we know of at present.
- (3) The use of filigrees is attended by a slight increase in the danger of sepsis.
- (4) Suppuration is not an indication for the removal of a filigree.
- (5) Wires displaced into a sinus should be removed without disturbing the filigree.
- (6) No belt or truss should ever be applied on the top of an implanted filigree.

(7) For the reduction of very large inguinal hernias and the avoidance of paralytic ileus the Trendelenburg position should be used, the abdomen opened, and the bowel withdrawn from within aided by pressure from without.

(8) In ventral hernias following appendicular abscess it is absolutely essential that the appendix be removed before implantation, if this has not been already carried out.

(9) Although in ordinary cases the lines I have elsewhere laid down with regard to the size, shape, and position of the filigree should be adhered to as closely as possible, it must be remembered that cases will arise which will tax to the utmost the ingenuity of the surgeon; in such cases hide-bound rules are worse than useless.

(10) It is important in dealing with gigantic hernias that every precaution should be taken for the comfort and safety of the patient. There must be skilled assistance, full facilities for asepsis, a good light and plenty of it, and, for choice, spinal analgesia should replace general anaesthesia.

Lastly, I am convinced that in view of the difficulty and danger of these operations they should be undertaken only by those whose practice renders them familiar with the technique of major surgery and who possess not only surgical skill but the gift of rapid manipulation.

## ANALYSIS OF CASES.

|  |     |
|--|-----|
| Total cases, 314, viz. :—  |     |
| Inguinal ... ..  | 263 |
| Umbilico-ventral ... ..  | 51  |
| Total implantations, 166, viz. :—                                      |     |
| Inguinal ... ..  | 106 |
| Double ... ..  | 20  |
| Umbilico-ventral ... ..  | 40  |
| Recurrences treated by implantation ... ..                             | 17  |
| Recurrences following implantation, 2, viz. :—                         |     |
| Inguinal, following suppuration ... ..                                 | 1   |
| Inguinal, following suppuration and partial removal of filigree ... .. | 1   |
| Recurrences following re-implantation ... ..                           | 0   |
| Filigrees partially removed for displacement of wires, 2, viz. :—      |     |
| Inguinal ... ..  | 1   |
| Umbilico-ventral ... ..  | 1   |
| Varieties of umbilico-ventral cases, 51, viz. :—                       |     |
| Umbilical ... ..   | 23  |
| Post-operative median ... ..   | 13  |
| Post-operative appendicular ... ..                                     | 14  |
| Epigastric ... ..  | 1   |
| Deaths from after-complications, 5, viz. :—                            |     |
| Ileus ... ..   | 2   |
| Broncho-pneumonia ... ..   | 1   |
| Pulmonary embolism ... ..  | 1   |
| Cardiac failure ... ..   | 1   |

## DISCUSSION.

Mr. JONATHAN HUTCHINSON said that Mr. McGavin had mentioned the efforts he had previously made to popularize the use of the filigree, and these had been read with interest on many occasions. He had, however, been waiting for exactly the kind of paper the author had given them that evening, embodying as it did a summary of his results. Most surgeons had admitted that the use of the filigree was an excellent method in certain cases, especially those in which there was a large gap in the abdominal wall, but the point upon which they wanted information was, as to whether the filigree stayed in without accident, and in how many cases suppuration and sinuses followed. Having congratulated him upon the paper, he would proceed to offer some friendly criticism. In the first place, it was difficult to make out from the paper exactly what number of cases were dealt with, and for how long a time they had been followed up. The first section of the analysis gave a total of 314 cases, and at first sight this figure might be mistaken for the number operated on. The figure 314, however, had very little bearing upon the subject, and meant simply the number of cases of hernia treated since the author had adopted in some of them the use of the filigree. The total number of implantations was 166, and what proportion of these cases had been followed up seemed doubtful. He took it that the figure included recent cases. But it was only after the lapse of two or three years, or, better still, of five or six years, that the results could be tested. He thought it a mistake to include any recent cases in such a table. Again, one wondered whether all these cases had been carefully and critically examined. The speaker had worked out some years previously the results of his own radical cures of inguinal hernia, dealing with a similar class of patients to those treated by Mr. McGavin—namely, East End labourers, who worked just as hard as his typical stoker. He included no cases of shorter standing than two years; in many cases ten years or more had elapsed, the average being six years. He found that 95 per cent. of these cases of inguinal hernia were soundly cured, so far as the particular hernia operated was concerned, and this result he would at once put forward in opposition to the statement of Mr. McGavin that “in filigree implantation is to be found the only true radical cure that we know of at present.” By following up these cases for many years every surgeon would find that although an excellent cure could be effected in the particular region operated on, there was a tendency to recurrence elsewhere. In the course of Mr. McGavin’s informal remarks while showing his slides, though not in his paper, he had referred to the risk of slight recurrence in the umbilical hernias, but this was hardly cognate. Patients would be found who had been cured of inguinal hernia, and in whom femoral hernia had subsequently developed, or an inguinal hernia might appear on the opposite side to the first. He found that such a form of recurrence had happened in a larger number of cases than that in which the hernia had recurred in situ. Not one of Mr. McGavin’s cases was recorded as having recurred elsewhere, although,

as he fully admitted, his cases included a larger number of what Mr. McGavin called "gigantic hernias"—the speaker thought the term hyperbolic—and therefore a good many recurrences elsewhere might be anticipated. He wondered, in view of this, whether the patients had all been carefully examined. So far as he could make out, there had been five deaths among these cases. Of course, it would be admitted at once that the percentage of deaths, suppurations, &c., was larger than in the average of hernia operations treated without filigree, and, indeed, Mr. McGavin had candidly pointed out that the risk of suppuration was greater. At the same time, he was dealing with exceptional cases; he had larger hernias than fell to the lot of the average surgeon, and the speaker thought the increased risk to life was fully justified by the success obtained. But he would point out that the proportion of cases of suppuration was very much larger than occurred in other methods. He attached great importance from this point of view to the use of kangaroo tendon for all deep sutures. He found that when properly prepared it never gave trouble. Mr. McGavin, out of 100 cases of inguinal hernia, had found it necessary to use the filigree in forty or fifty. The speaker had looked up the records of recent operations for inguinal hernia at the London Hospital, and had found that he and his colleagues had only used the filigree once in 100 cases. Mr. McGavin's statement that the use of the filigree was the only radical cure for hernia was an exaggeration. So far as the context went, the statement seemed to apply both to inguinal and ventral hernia. If he had said that filigree implantation was an admirable method in very large hernias, he would have found general agreement, but the statement as it stood should be modified. He heartily congratulated Mr. McGavin on his results, and thought the record of them would encourage a larger use of filigree.

Mr. STANLEY BOYD thought that all must have been struck with Mr. McGavin's great success in a series of exceptionally bad cases. It would be interesting to learn how he obtained so many bad cases. Doubtless it was for such cases that Mr. McGavin felt that filigrees were the only radical cure. It was evident also that Mr. McGavin had followed up a large proportion of these cases for a sufficient length of time to obtain fair proof that a radical cure had been effected. If, as Mr. Hutchinson had pointed out, Mr. McGavin had not reported the recurrence of hernias in other places, the absence of such recurrences was probably due to the fact that he had used the wire grid. The only recurrence of this kind (due to the operation performed) which had troubled the speaker was a bulging in front of the femoral vessels owing to pulling up of Poupart's ligament after Bassini's operation. If the conjoint tendon was sewn to Poupart's ligament under any tension, this bulging might result; but the speaker had not seen more than a bulge. That should not happen with a wire grid, because the soundness of the defence depends much less upon accurate approximation of parts. He agreed with Mr. Hutchinson as to the inaccuracy of the remark that filigree implantation was the only radical cure for hernia. They must all have had radical cures in a large proportion of cases

of hernia in which they had done the ordinary operation: but this did not apply to very large hernias. He had not seen the last form of grid which Mr. McGavin showed on the screen—the one, namely, with the three backbones. Some arrangement of the kind was very important, for the speaker, like other people, had felt that the ordinary grid did behave, as Mr. McGavin had said, like a mass of fish-bones. He had wondered whether he surmounted the difficulty by means of very free incision, or had some other method of avoiding the trouble. He had been led to try some other materials, one of these being a bit of Kodak film, which, with a few holes punched through it, was easily cut into the exact shape required, and could, he thought, be buried with perfect safety. He had used it—but only in a few cases—for three or four years with no untoward results.

Mr. ARTHUR E. J. BARKER congratulated Mr. McGavin upon his very frank exposition of this procedure, and personally he was not inclined to quarrel with the expression "gigantic hernia." The hernias of which Mr. McGavin had shown the photographs were certainly very large indeed. He expressed himself also entirely in accord with the treatment given in such cases. His own experience of wire networks of one form or another, used for the purpose of operations on the abdominal wall, dated back for a considerable time. He had been formerly accustomed to make a network on the spot, threading the fine silver wire to and fro across the aperture, and had found it of great service in his early cases. He had then been inclined to use rather thicker wire for strengthening the tissues than appeared now to be necessary, and latterly, in order to get rid of the drawback of making the network on the spot he had used filigree of one kind or another. His own differed in certain respects from that described by Mr. McGavin, but it was more handy than making the network in the wound. The method as applied to ventral hernia was an exceedingly good one. There were ventral hernias which were very difficult to control in any other way, and he knew of no method so good as that of interposing between the rectus and the fascial part of its sheath one of these filigrees. For inguinal hernia he thought its use should be more exceptional. The vast majority of such cases, even when the hernia was very large, could be controlled by Bassini's operation if proper attention was given to detail. For the ordinary case, such as they had in the hospital every day, he did not think filigree was at all necessary. He did not know whether it was quite fair to Mr. McGavin, whose work he so much admired, to modify his filigree, but he had used it bifurcated, to some advantage occasionally. While feeling that in this class of ordinary inguinal hernia the use of filigrees should be considered as exceptional, he thought it exceedingly valuable as a means of resort in the large varieties, while in many cases of ventral hernias he did not quite see what else could be done. He described a case which he had shown before one of the societies two or three years ago, and in which he felt himself to be non-plussed. It was that of a man, aged 37, who had a large suppurating mass growing out of his umbilicus. The mass was undoubtedly carcinomatous, and

had grown through the umbilicus to the extent of his fist. The case was one of carcinoma of the transverse colon, infiltrating the abdominal wall as well as the skin. No tissues were available with which to close up the wound. He excised the transverse colon and made an end-to-end junction, but found it almost impossible to keep clear of the foul external wound. There was a little suppuration, but this healed. Nothing except a thin trace of the peritoneum, however, and a thin scar remained to defend the stretched part of the abdomen. At the next intervention he cut out his old scar and laid in filigree, splitting the right rectus and drawing it in strands over the gap. The patient recovered, presented himself without hernia, and said with considerable pride that he now played golf regularly. The question of recurrence in other places had been raised by one or two speakers. The fact that after operating on one hernia, a hernia should appear on the other side of the body was explained, in his judgment, by the bad tissues and the tendency to hernia which was characteristic of these patients. After the relief of one hernia, therefore, making a good, sound cure, hernia might appear elsewhere as a consequence of increased exertion on the part of the patient, quite irrespective of anything that had been done to him. The best thing to do was to cure the hernia that was in evidence, and to take the chance of such a recurrence. They could safeguard themselves by telling the patient that although they could relieve his present hernia he might subsequently develop hernia on the other side.

Mr. JOCELYN SWAN described his personal experience of a case which illustrated the great use of an implanted filigree. It was a case of large malignant tumour of the rectus abdominis muscle involving a part of the peritoneum and the posterior aponeurosis. The abdominal cavity was opened, and a piece of the peritoneum some 2 in. wide was removed with the tumour. There was some difficulty in getting a proper abdominal wall, but he was able at the time to implant the filigree directly upon the stretched portion of the peritoneum, and to bring the anterior rectus aponeurosis over it. The wound showed a very good result. The time was not sufficiently advanced to speak of the permanence of the cure, but for four months the woman had had a perfectly sound scar and a perfectly sound abdominal wall. He had used filigree in cases of ventral hernia with extremely good results, and three patients, after four years' interval since the operation, had not developed hernia in any other position. The good effect of using a filigree in the case he had mentioned was an additional testimony to its advantages.

Mr. SIDNEY BOYD referred to the fact that Mr. McGavin was the pioneer surgeon in the use of filigree in cases of hernia in this country, and said that personally he had found the filigree of the greatest service in those cases of direct inguinal hernia which came on in middle-aged and elderly people. He related a case of double inguinal hernia, in which on the right side the hernia was large, the gap admitting three fingers. On that side he used a filigree. On the left side the hernia was quite a small one, and here he employed a



method of approximation, guarding the hernial gap without filigree. In six months or so the patient came back, when it was found that what had been the bad side was absolutely sound, while the treatment on the other side had been a failure. Thereupon he put in a filigree on the left side, and the patient had since done very well. With regard to the question of sepsis, it was comforting to hear that this did not affect the final result very much, but he thought that Mr. McGavin had been rather fortunate in his cases. Mr. Stanley Boyd had mentioned the recurrence of the hernia through the small incision which was made to bring up the invaginated sac through the abdominal wall. The speaker had encountered a similar difficulty in dealing with femoral hernia, and he would like to know whether Mr. McGavin had found any means of using the filigree in cases of bad femoral hernia. There was no doubt that hernia, relieved on the one side, might recur on the other, and he quoted the remark of a patient, a clergyman, "Thank God, man has only got two sides to his body!"

Mr. W. McADAM ECCLES said that these cases must be divided definitely into two classes—namely, umbilico-ventral hernia and inguinal hernia. The term "abdominal hernia" was not admissible, seeing that all hernias spoken of were abdominal. The speaker thought that there were few cases of inguinal hernia in which filigree was necessary. Almost all inguinal hernias, even the huge or gigantic hernias, could be definitely cured without a filigree provided the patient was a suitable one to undergo a severe operation. But when one came to umbilico-ventral hernia it was a different matter. In cases of huge hernias of this type the filigree might be useful, but the great difficulty was the reduction of the contents of the sac and the prevention of the various complications that Mr. McGavin had brought forward. Of course, the real answer to the question was never to let these cases reach so bad a stage, and the future generation of surgeons, he hoped, would not have them to deal with. There was one question that he would like to put to Mr. McGavin. It had reference to a class of cases already mentioned, in which a definite portion of the muscular tissue of the abdominal wall had to be excised. The difficulty in such cases was to obtain sufficient bed for the filigree to lie in. He understood from Mr. McGavin's paper that he placed the filigree directly upon the extraperitoneal tissue. What would he advise to be done under conditions in which this was not sufficient? In one case of his own he brought the peritoneum together as well as he could and placed the filigree upon the intestinal wall, and in one or two cases, subsequently, he brought portions of the abdominal wall over the filigree. What was the real value of such filigree in a hiatus of the abdominal wall? Was it simply the scar tissue which was caused by the filigree? Scar tissue without filigree, he thought, was not altogether good, but scar tissue plus filigree certainly was. He added that once or twice a year he had to remove filigree which had been put in by other surgeons, and once one which had been put in by himself.

Mr. ARTHUR BARKER added, that in his own belief, the filigree not only did not irritate a septic process, but seemed to control the infection, and after a while, as in the case which he had described earlier in the discussion, one could see in the exceedingly thin scar strands of the wire exposed here and there without irritation around. The man had now nothing in the upper part of the wound but the scar, and it was holding as he did not think any other scar would have done, although some of the fine wires had been drawn out.

Mr. STANLEY BOYD asked, with regard to a statement made in the paper as to the aseptic nature of the silver wire, whether it was not held that copper was more strongly antiseptic than silver.

Mr. MCGAVIN said that he had used copper wire in bone operations. He found it produce, however, not an actually suppurative condition, but a local necrosis in soft tissues with the formation of verdigris. Almost always it ultimately produced a chronic sinus.

The PRESIDENT (Mr. G. H. Makins, C.B.) remarked that copper wire was used in St. Thomas's Hospital for patellas without producing any trouble so far as he knew.

Mr. MCGAVIN, in reply, said, in the first place, that the list he had furnished in his paper did not exhaust all his cases. His paper was originally intended to be read at the Annual Meeting of the British Medical Association at Liverpool, in July, and was finished off in the earlier part of 1912. Cases treated since that time were not represented in the report. He would ask Mr. Hutchinson to remember that his cases went back to 1904, and if eight years was not sufficiently long to wait for the possibility of recurrence? As to the doubts thrown upon the critical nature of the examination in these cases, he could only say that he took the greatest pains to find out the patients. He sent out postcards to all of them, some to very distant parts of the world, and he received 68 per cent. of answers, everyone who replied being perfectly well. His statement that filigree implantation represented the only true radical cure for hernia had been criticized. He would retract it in deference to Mr. Jonathan Hutchinson, but what he meant was that in the class of hernia he was dealing with, this was the only method in which, if nothing unforeseen occurred—if, for instance, the result was aseptic—a cure could be absolutely guaranteed. Bassini's was an excellent operation, but he was confident that if the contents of a hernia of no matter what size could be got back with filigree on the top, the result would be more radical in character than that obtained by any of the ordinary methods. He wished to dissent strongly from Mr. Hutchinson's remark that no cases of hernia were so large that they could not be cured without filigree. [Mr. HUTCHINSON said that he was referring to inguinal hernia.] Mr. McGavin said that he dissented from the statement even in the case of inguinal hernia. If he might say so, he could have put before the Section at least two dozen cases which had come to him after repeated operations by particular surgeons—some of them having

been operated on as many as six times before they came into his hands. The reason why he had got so many bad cases was because he went out of his way to get them. He had deliberately sought out bad cases for the purpose of testing the method. Mr. Stanley Boyd had mentioned the danger of tightness of suture. A good many of the cases of recurrence were due to the unwise attempt to bring down the conjoint tendon when there was no conjoint tendon to speak of to bring down, and to tying sutures too tight. But if a filigree could be put in there was something to show for one's efforts—something to make a scaffolding on which new fibrous tissue would form. He was interested to hear Mr. Stanley Boyd's use of Kodak film, and he would like to ask him how he sterilized it. Providing there was sufficient through-and-through anastomosis of the vessels, there seemed to be no reason why it should not act, but the sterilization was a matter of the greatest importance. [Mr. STANLEY BOYD said that he sterilized it by immersing it for a short time in carbolic acid, 1 in 20.] Mr. Barker had raised the question as to whether there was any actual necessity for inguinal hernia to be treated by filigree. The speaker thought that it was only in exceptional cases that one needed to use filigree. The question as to the appearance of hernia on the other side rather brought one back to Hamilton Russell's theory. The speaker did not see why an operation, when well performed, should deliberately give rise to a hernia on the other side of the body. He believed that the majority of hernias were not acquired at all. The true cases of acquired hernia were those of direct hernia in elderly people, hernia acquired as a result of previous ill-advised or ill-conducted attempts at operation, and hernia following sepsis or other faulty technique. With regard to suppuration after filigree, he reminded them that in suppurating appendicular wounds Bartlett had put in filigree deliberately, the suppuration taking place around it, and an extremely strong abdominal wall was obtained. Mr. Sidney Boyd had mentioned the question of femoral hernia. The speaker had given up attempts at filigree implantation in this class of case, because personally, in spite of what the text-books said, he did not think that femoral hernia ever recurred. If femoral hernia were treated in the ordinary way, the sac being tied high up, and one made sure that one had got rid of all lateral sacculi, he had never found hernia coming down into that region again. With regard to the removal of filigree, he considered that no filigree should be removed unless a wire was displaced into a sinus, when removal should only apply to such wire or wires. Care was required in obtaining the proper silver wire, which should be of 28 standard wire gauge. The reason why removal became necessary was frequently that too heavy wire had been used. He had known of wires being implanted which were unbendable, and hæmorrhage and sinus formation would always be produced under such circumstances. If put in properly, however, and the proper thickness of wire employed, there was no need to remove the filigree even in the presence of suppuration. With regard to the point raised by Mr. McAdam Eccles as to the making of a bed for the filigree in the absence of sufficient peritoneum, he had tried on one occasion the sewing into the gap

of the omentum, but, unfortunately, the omentum did not possess sufficient strength to hold up the filigree. When one saw the enormous amount of adhesions that some patients developed and could live through, he did not see that the making of one or two others by sewing intestine into the gap was likely to be a serious matter. A bed would thus be formed for the filigree as in the case he had already mentioned. Peritoneum should not be stripped from the sheath of the rectus muscle as in Bartlett's original method, on account of its liability to tear; it was easier and better surgery to separate the muscle from the posterior layer of its sheath and implant the filigree between them.

## **Surgical Section.**

January 14, 1913.

MR. G. H. MAKINS, C.B., President of the Section, in the Chair.

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### **Actinomycosis, with Special Reference to Involvement of Bone, and an Account of a Case primarily involving the Inferior Maxilla.**

By A. G. HAYNES LOVELL, F.R.C.S.

CASES of actinomycosis of bone are sufficiently rare and difficult to diagnose to excuse me recording the following case, in which the extent of the lesion, though early and small, is seen in the skiagram very kindly taken for me by Sir James Mackenzie Davidson. I can find no skiagrams illustrating the condition in the literature of the subject.

#### **REPORT OF THE CASE.**

The patient was an Oxford graduate, aged 23, still up at Oxford, and working very hard for a high examination which was followed by a "medical examination." On July 20 he complained of trouble in his gum around the left lower canine—there was no apparent cause. This was followed in a few days by pain in the first molar, so its stopping was removed and an attempt made to kill the nerve with an arsenical dressing. Owing, however, to persistent pain, extraction was performed. A few days later there was more pain; a thermal test was then applied to the second bicuspid, after removal of its stopping. There was no response, so the dentist explored the tooth and found a live pulp. The tooth was extracted. The two teeth extracted showed no signs of disease except superficially. A week later the patient noticed slight swelling of the jaw externally in this region. The lump got progressively larger, and there was a persistent dull pain till August 12, when I first saw him and received the above history from his Oxford dentist who had been much puzzled by the case.

Condition on August 12, 1911: The patient did not look very well. His temperature was 99° F. There was a mass the size of a walnut fixed to or part of the inferior maxilla on the left side. Its limits were ill defined. It was hard, and the skin over it was slightly red and oedematous. There was but little pain. Inside, the mouth was very clean, with a healthy granulating wound over the site of the extracted teeth. There was no sinus discharging into the mouth, but the probe through the granulations touched bare bone. As regards the diagnosis, the following had to be considered:—

(1) Periostitis associated with a sequestrum or a stump. This seemed the most probable as being common, but there was no sinus into the mouth as is so frequent in these cases.

(2) Dentigerous cyst or follicular odontome. In this case I should have expected the expanded condition to have been perceptible from within the mouth as well as from without, and constitutional change would have been absent.

(3) Epithelial and other odontomata. Here again I should have expected a more uniform expansion of bone than was present.

(4) Sarcoma was quite a possible diagnosis.

(5) Chronic osteitis or periostitis due to syphilis, tubercle, chronic sepsis, or actinomycosis. The first of these was excluded.

Accordingly Sir James Mackenzie Davidson kindly took a photograph for me (fig. 1). It shows definite rarefaction of the bone and suggests an abscess at the root of the first bicuspid. It also shows absence of new bone formation, periosteal or otherwise, and of bone expansion. In fact, it left me with the diagnosis of chronic inflammatory trouble of unknown origin. After consultation with a dentist I explored (under eucaïne) from the sulcus between the alveolus and the cheek, but found no pus. In a day or two a further dental opinion was taken. The three teeth in front of those extracted were found to be loose, while sensation in the first bicuspid was present though much diminished. Arsenical necrosis was suggested as a possible diagnosis. Next day there were signs of pus, so I made a small incision under the jaw and let out a very little thin pus. Films of this showed pus cells but no organisms. Agar slope cultures were made from the wound and were incubated aerobically. The wound was dressed and fomented daily. Nothing showed on the cultures till the eighth day, when four small, white, heaped-up, round, opaque colonies appeared. These on examination showed a Gram-positive, non-acid-fast streptothrix. This led me once more to examine the now very scanty discharge from the sinus. In it I found

a few sulphur granules which showed the organism. On August 24 I started giving the patient potassium iodide, 15 gr. three times daily, and on September 1 the first dose of autogenous vaccine was given. Mr. Fleming, of St. Mary's Hospital, kindly made the latter. It contained approximately 80 million fragments of the mycelium per 1 c.c., and the first dose was  $\frac{1}{4}$  c.c.

On September 5 a small incision was made under the jaw on to the bone. The periosteum easily stripped up and some carious bone was scraped away. The wound healed except for a small sinus. The potassium iodide was increased to 30 gr. three times daily, and the patient continued to receive inoculations with the vaccine at ten-day



FIG. 1.

Actinomycosis of inferior maxilla; the arrow points to a small clear area suggestive of an abscess cavity.

intervals till December 9 when I saw him again. The swelling was very much diminished in size, but a sinus still persisted.

Sir James Mackenzie Davidson kindly photographed the patient again. The picture shows much less rarefaction than was present in the first skiagram, but there is still a small area suggestive of an abscess cavity at the root of the first bicuspid. A probe in the sinus is seen stereoscopically to pass up internal to the mandible. Because of the area at the root of the first bicuspid I recommended persistence with the treatment.

On February 16 the difference on the two sides was only perceptible on the very closest examination, and I think the patient may now be



regarded as cured. He passed his medical examination in November unchallenged, though several consultants said in August that he had no chance at all.

It is now sixteen months since treatment ceased, and he is still quite well.

#### THE PATHOLOGY AND COMPARATIVE PATHOLOGY OF ACTINOMYCOSIS OF BONE.

Usually when bone is involved by this organism it is by direct extension from a previous extensive focus in the soft parts. The only region where an *apparently* primary disease of bone occurs in man is in the jaws and here the evidence, that is attainable, is in favour of direct infection from the oral cavity through the sockets of carious teeth. Primary bone lesions have never been produced experimentally and metastases are much rarer in bone than in the soft parts. Two cases of isolated areas of infection in bones other than in the jaws are reported, one in the lower epiphysis of the femur (Israel), the other in the upper end of the tibia (Kohler). By a false likeness to the "lumpy-jaw" of cattle, writers in the past have often recorded in man as osseous disease what is really disease of the soft parts adherent to adjacent bones. In the region of the jaw in man we meet with:—

(1) Disease of soft parts with periostitis of adjacent bone.

(2) Disease of bone by invasion of it with the organism, infection reaching the bone from the surface, and then (a) eroding the bone gradually from the surface towards the medulla, or (b) reaching the medulla early, the inflammatory process progressing there in excess. This type is often combined with a great increase in bulk of tissue simulating osseous hyperplasia.

The best clinical description of actinomycosis in man is by Poncet, of Lyons. In his exhaustive treatise he describes three clinical types of the disease affecting the inferior maxilla:—

(1) A peripheral rarefying process, of which definite cases seem to be rare.

(2) A central perforating type, the commoner type in man.

(3) A central neoplastic type, the commoner type in cattle.

The case I report is one of the second type. Poncet says parchment crackling and spontaneous fracture may occur in such, but usually the bone is perforated in several places, whence the process tracks in the surrounding soft parts, chronic sinuses resulting. In the lower jaw the

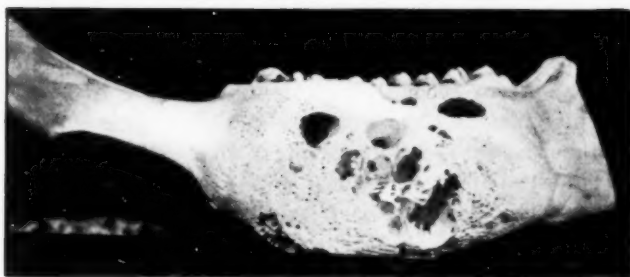


FIG. 2.

Inferior maxilla of ox showing changes typical of the neoplastic type of actinomycosis.



FIG. 3.

Skiagram of the bone shown in fig. 2.

amount of bone involved is usually small, but in the upper jaw it is frequently very extensive. On scraping the bone carious spicules are found, rarely or never sequestra of any size. One case with a large sequestrum is reported (Fevrier). Toothache is an early symptom, and subsequently the teeth become loose. I may say here that diminished sensibility of teeth to heat and X-ray evidence are important in diagnosis. There is little or no true bony thickening in these cases. When it occurs at all it is periosteal and very slight in degree.

The third clinical type, the neoplastic one, is quite common in animals but rare in man. Further, when it occurs in man it is never so extreme as in animals. The tumour has been called "*ostéo-sarcome mycosique du boeuf*." There is vast increase in bulk. The bone is surrounded by and merges into a hard mass of unequal consistence. The overlying skin is ulcerated in several places—chronic sinuses resulting. On section the mass is grey and gristle-like, with many yellow spots, each the size of a pin's head, in which one finds the organisms.

Fig. 2 shows the inferior maxilla of an ox affected with the disease, after maceration, and fig. 3 is a skiagram of the same (*see* p. 125).

When a specimen is macerated and the bone itself studied, it shows symmetrical expansion, the expanded area forming an appreciable bulk of the original tumour. It is thinned out and traversed by many large tunnels which reach the surface through many large cloacæ. The lamellæ of bone throughout the mass are of delicate structure especially peripherally. There evidently have been two processes at work, namely, rarefaction, passing to a kind of caseation, and periosteal new formation, leading to expansion. The former is in excess of the latter, which is apparently one of Nature's efforts to limit the process—an effort which seems lacking in the case of man.

Before closing I should like to emphasize the importance of early diagnosis. There is at present only one way of being certain, and that is to find the organism. As this case shows, a negative finding on the first occasion by no means decides against a case being due to actinomycosis. It is only a demand for a further examination. An early diagnosis means less need for radical surgery, and literature shows how very much better cases react to potassium iodide, given and tolerated in huge doses, in the early stage of the disease.

In conclusion, I wish to thank Sir James Mackenzie Davidson for his kindness in taking the skiagrams shown.

I should like to ask for the opinion of Fellows of this Society on the advisability of surgical interference in such an early case as this. I feel

that potassium iodide in very large doses and vaccines should be tried before surgery is thought of in any case where there is no evidence of secondary infection and where the patient can be closely watched. In my opinion, evidence of extension of the lesion under such medical treatment should be the earliest indication for surgery. I think this case would have got well without operation.

### **Some Clinical Features of Actinomycosis.**

By THOMAS H. KELLOCK, M.C.

THE disease, actinomycosis, or streptotrichosis, has either become more common during the last few years or has been more frequently recognized, for its occurrence seems to be more and more frequent, and amongst hospital out-patients cases of it present themselves so often that one has always to bear it in mind when discussing diagnosis, yet, up to quite recently at any rate, one met with cases reported in the medical journals as if they were still rather of the nature of curiosities. One finds it occurring in people of all classes of society, in both sexes, at all ages, and in persons of the most varied occupations; affecting as it does town-dwellers as well as those who live in country districts, it would seem that the organism in some of its varieties had ceased to exist, as was formerly believed, solely on grass, hay, and straw, and, like the bacillus of tuberculosis, to which, in some respects, it bears so close a resemblance, became almost ubiquitous.

Having, during the last few years, met with quite a large number of cases of this affection, I thought it might be of interest if, as my contribution to this discussion, I were briefly to review some of the clinical features it presents in various parts of the body; it is by them that the immediate diagnosis has generally to be made, for the difficulties of a certain microscopical or bacteriological confirmation seem sometimes to be great, and I have on several occasions only had a positive result after several negative examinations had been made. I suppose an explanation of this may be found in the important fact that one meets with the disease under two very different conditions: the simple or clean, and those in which a septic infection has been superadded, and, as in the case of tuberculosis, it seems difficult to demonstrate the organism in the presence of the latter.

As regards the mode of entry into the body, probably every case

is infected through either the alimentary or respiratory tracts, for it is in direct connexion with these that one almost always meets with it; that it may be carried by the blood-stream and so to organs that do not connect directly with these tracts is shown by its occurrence in the kidney. Once inside the cavities of the body, the organism seems to have a peculiar tendency to insinuate itself into ducts that open on the surface, and progressing apparently against the stream of the natural secretion, infect the organs from which these ducts come, and thus the salivary glands, liver and vermiform appendix are frequent seats of its manifestation.

The mode of spread when once the disease has become established is somewhat curious, for, contrary to what has been stated, my experience has been that it rarely spreads by means of the lymphatic circulation, and it is very rare to find lymphatic glands affected. Its preference seems to be to spread by direct continuity of tissue and, unlike tuberculosis in this respect, to ignore anatomical boundaries and cause adhesions by invading all and every structure with which it comes in contact; its behaviour in this respect only resembling that of malignant disease. The way in which a pulmonary focus will cause adhesions to the pleura, an invasion of the chest wall, and a superficial abscess without empyema, is a good example of its method of spread.

It has generally been supposed that the portal vein was the means of conveying the organism to the liver when that organ had been found infected, but, as I tried to show in a paper I read a few years ago at the Medical Society of London<sup>1</sup> on some cases of this affection of the vermiform appendix, it seems more than likely that the hepatic infection is an independent one direct from the duodenum, and a case I reported in which the vermiform appendix, liver and pancreas were all found to be affected helps to prove this contention.

For the purposes of this paper I am relying solely on cases that have come under my own notice; very possibly some of those present will be able to add to them as far as the different parts of the body are concerned, for no part or structure would seem to be immune.

When the disease attacks the *lower jaw*, a situation in which it so often occurs in cattle, the most marked feature is its painlessness as compared with that of a septic infection of the same part. Often the first indication is a small red, puckered swelling on the face, preceded possibly by a slight toothache or merely a feeling of tension; the spot

<sup>1</sup> *Trans. Med. Soc. Lond.*, 1907, xxx, pp. 15-26.

enlarges, is found to be adherent to the bone, softens in the centre, and, if incised, is found to contain very little pus. If it is a small isolated spot it is seldom followed by necrosis and will often get perfectly well without any treatment beyond an incision. In one case where the ascending ramus was affected there was a large swelling on the side of the face which had been increasing in size for many months, without much pain but with marked fixation of the jaw, and in this case was followed by the shedding of several small sequestra. The case was that of a gentleman from the country, an ardent sportsman who spent nearly all his time in the fields, and several of the teeth in his lower jaw had been extracted on the supposition that the affection was a septic one.

It is odd how rarely the *upper jaw* seems to be affected. I have never myself met with a case in that situation. In three cases I have found the disease affecting the *centre of the cheek*, appearing first as a red, puckered spot, and increasing slowly and painlessly. In these cases I believe the infection is through the opening of the parotid duct, for they have all been at the spot on the face that corresponds to that opening internally. In one of the cases sepsis had been superadded, and the whole side of the face was swollen, red, tender, and suppurating, and it was only after this had subsided under incisions that the streptothrix fungus was demonstrated.

An infection of the various glands whose ducts open into the mouth is very common, and I have found it in the parotid, submaxillary, and sublingual glands. In one case of submaxillary infection the duct itself was affected as well as the gland, and the case—that of a gardener from Hampshire—was brought to me as being one of epithelioma of the floor of the mouth with secondary lymphatic glands. The tissues of the neck, however, very rapidly softened, and an incision and examination of the pus proved the real nature of the disease. In a case of sublingual infection the patient, when first seen, had all the tissues in the front of the neck and over the front of the upper part of the thorax infiltrated, the neck fixed, and the chin drawn nearly down to the sternum: it had started, he said, as a small swelling just under the front of the lower jaw.

In two cases I have seen the disease in the *tongue*; in both it affected the deeper parts and there was no ulcer on the surface; a rather soft, circumscribed, painless swelling of rather rapid increase in size without interference with the movements of the tongue, were the chief characteristics. In one case—that of a London lad who was an in-patient at the hospital for another condition—I mistook it for a mucocele; in the other, a farmer, it had been thought to be malignant and the patient advised to have the tongue removed.

Affecting the *tissues of the side of the neck*, the most noticeable features are the marked fixation it causes and the manner in which it spreads backwards, sometimes to the middle of the back of the neck. One of the first cases I ever saw was in this situation; the patient was a gentleman who had just returned from Persia. He had a large infiltration of the left side of the neck extending from just below the ear to the clavicle; painless, but causing much inconvenience from fixation. On operating I found all the structures in the neck involved and removal practically impossible. At the time I thought it must be sarcoma, but the wound healed and microscopical examination was very doubtful; it was only when later a small abscess formed in the scar and the escape from this of typical pus containing yellow granules that the true nature was recognized. Quite lately I had two patients in the Middlesex Hospital at the same time with diffuse infiltration of this kind affecting the whole of the side of the neck with sepsis added in both cases.

When the *lung* is the seat of the primary infection, adhesion to the chest wall often occurs rapidly and in this way one meets with chronic abscess at almost any part of the chest wall; under the breast, in the axilla, or just under the clavicle, seem the most common places. Here, too, the painlessness of the affection is often noticeable, and if the pulmonary infection is a slight one the patient is often apparently in good health, although, as I saw on one occasion in quite a young child, a large part of the chest wall, including ribs, muscles, and skin, may be infiltrated and showing many ulcerated and discharging points.

Many cases of the disease affecting the *vermiform appendix* and *cæcum* have been recorded, and for the paper I have referred to I was able to collect quite a fair number from the records of the Middlesex Hospital alone, two of which had been under my own care. Noticeable features in these cases had been the large amount of infiltration with comparatively little breaking down in the clean cases, and the curious behaviour of the abscesses when such occurred, lifting up the iliac vessels and infecting the psoas muscle in one case, coming to the surface in the middle line above the umbilicus in another.

Perhaps the most interesting of all my cases was one I reported some years ago when the *right kidney* was the part affected. The patient, a young woman, had a large tumour of the kidney which was movable; pyuria and pyrexia were present, and I removed the kidney, thinking it to be tuberculous, but on examination the disease in it proved to be actinomycosis, and after prolonged treatment with large doses of iodide of potassium she was well and without any further evidence of the



disease for, at any rate, three or four years, since when I have lost sight of her.

In all these cases the diagnosis was confirmed by bacteriological examination; in two cases, the one in the clavicle, the other in the pelvic bones, I thought the clinical evidence and progress of the case after treatment almost conclusive, but no confirmation could be obtained. In the case where the clavicle was affected the patient, a young man, had a chronic enlargement of this bone which was thought to be sarcomatous, whilst in the hospital acute inflammation occurred in it and spread to the surrounding structures. After incisions and scrapings, followed by large doses of iodide of potassium, he completely recovered, but, as I have said, no confirmation of the diagnosis could be obtained.

The affections for which I have mistaken this disease and known it mistaken by others have been: *Streptococcal* infections in cases of the lower jaw and salivary glands; *tuberculosis* in the case of the child with the affection of the chest wall and in the renal case; *sarcoma*, as in the tissues of the neck and possibly in the case of the clavicle; *carcinoma* in the tongue and floor of the mouth; for *gumma*, and in one case for salivary calculus.

To sum up the chief clinical features of this disease, these are, I think: Its existence under two conditions, the clean and the septic; its comparative painlessness; the rather curious linear puckering which it causes in the skin; the way in which it infiltrates all the surrounding structures, disregarding anatomical boundaries and causing adhesions; its disposition to enter ducts opening on to a mucous surface; the very little pus that is evacuated even when what appears to be a collection of some size is opened; the rapid improvement that takes place after scraping and the administration of sufficiently large doses of iodide of potassium; and, lastly, the remarkably little deformity or disfigurement that results after treatment has succeeded in eradicating it.

**Some Observations on a Series of 78 Cases of Streptothrix Infection.**

By ALEXANDER G. R. FOULERTON, F.R.C.S.

By way of contribution to a discussion of streptothrix infections, I thought that it would be worth while to refer to some points in connexion with a series of cases which have been investigated in my laboratories at the Middlesex Hospital, and in which the presence of the causative parasite has been demonstrated positively by laboratory methods.

In the Milroy Lectures "On the Streptotrichoses and Tuberculosis" in February, 1910,<sup>1</sup> I was able to refer to fifty-three cases of the kind which had been investigated at the Middlesex Hospital during the preceding ten years. During the last three years twenty-five additional cases have been examined—thirteen cases of primary infection of parts about the mouth and neck, six cases of primary infection of the appendix, five cases of pulmonary infection, and one case of cystitis. The series, therefore, now includes seventy-eight cases. A very large majority of these have occurred in the routine of hospital work, and material from the remainder has come from cases outside in which I have been consulted. If the generally prevailing idea as to the comparative rarity of streptothrix infections were correct, this series of seventy-eight cases investigated in one laboratory during a period of thirteen years might seem exceptional, since Acland, who, in the year 1884, identified the first case of human actinomycosis recorded in this country, was able to collect only 109 British cases published during the twenty-three years 1884-1906. But it is certain that, excluding for the time all cases diagnosed as cases of tuberculosis, cases of streptotrichosis are much more common than the number of recorded cases would lead one to believe. And I am convinced that my own series of seventy-eight cases, observed during thirteen years, understates very seriously the frequency of occurrence of cases of streptotrichosis in ordinary hospital practice. The series includes only cases in which either a streptothrix was obtained in culture on artificial media, or in which typical branching mycelium was identified in stained specimens of material. Had cases in

<sup>1</sup> *Lancet*, 1910, i, pp. 551, 626, and 769.

which there were found what were almost certainly rod forms and spores of a streptothrix been included, the list would have been considerably longer. The number of cases of appendix infection, for instance, would have been increased largely. The question of the microscopic demonstration of streptotrichæ will be referred to later on. Meanwhile, I may deal with the question as to whether there is otherwise any reason for believing that our results at the Middlesex Hospital are in any way exceptional, in the sense that they do not represent the average of hospital practice.

In order to test the value of any special series of cases, the best method is that of comparison of the individual result with the collective results of others. If the outcome of individual experience coincides nearly with the outcome of collective experience, then the individual experience may be taken as representing fairly the normal average. I will therefore collate the Middlesex series of cases with series of cases collected elsewhere by the following tests: (1) As to age-incidence; (2) as to sex-incidence; (3) as to the influence of occupation on incidence; and (4) as to the more frequent sites of primary infection.

In the matter of sex-incidence, the Middlesex series of 78 cases may be compared with one of 405 cases collected by Leith,<sup>1</sup> and with Acland's series of 109 cases, in which sex is stated in 101.<sup>2</sup> It will be seen that the figures of the Middlesex series coincide nearly exactly with Acland's, whilst Leith's figures show a somewhat higher prevalence amongst males.

|                          | Number of cases |     |     | Sex percentage |     |      |     |      |
|--------------------------|-----------------|-----|-----|----------------|-----|------|-----|------|
|                          | M.              | ... | F.  | M.             | ... | F.   |     |      |
| Leith (collected cases)  | ...             | 295 | ... | 110            | ... | 72.9 | ... | 27.1 |
| Acland (collected cases) | ...             | 65  | ... | 36             | ... | 65.0 | ... | 35.0 |
| Middlesex Hospital       | ...             | 51  | ... | 27             | ... | 65.4 | ... | 34.6 |

In the matter of age-incidence, the Middlesex cases correspond closely with those of Acland's series. The age is stated in 84 of the latter, and was ascertained in 70 of the former.

|                              | Total | Under 25 | 15 and under 25 | 25 and under 35 | 35 and under 45 | 45 and under 55 | 55 and upwards |
|------------------------------|-------|----------|-----------------|-----------------|-----------------|-----------------|----------------|
| Acland's collected cases ... | 84    | 12       | 24              | 25              | 9               | 7               | 7              |
| Middlesex cases ...          | 70    | 6        | 23              | 19              | 9               | 11              | 2              |

<sup>1</sup> *Edinb. Hosp. Reports*, 1894, ii, pp. 121-91.

<sup>2</sup> I have to express my thanks to Dr. Acland, who has very kindly provided me with the details of the 109 collected British cases which are referred to in his monograph on actinomycosis in Allbutt and Rolleston's "System of Medicine," 1906, ii, part 1. Dr. Acland wishes the full share of Dr. P. S. Hichens, of Northampton, in the work of compilation of the series to be acknowledged.

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In Acland's series, forty-nine of the cases, or 58·3 per cent., occurred between the ages 15 and 35; in the Middlesex series forty-two of the cases, or 60 per cent., occurred within the same age-period.

The influence of occupation on the incidence of infection is an interesting subject for consideration in connexion with the pathology of streptotrichosis. From the first it has been recognized that infection may be carried to man and lower animals by means of straw and grain. That fact was established by clinical observation; it was afterwards found that, when not living as parasites on man and other animals, the streptotrichæ are essentially either saprophytes living in the soil, or parasites of higher forms of vegetable life. And it is well known that acid-fast species which closely resemble in many ways Koch's *Bacillus tuberculosis* occur as natural parasites of grasses and other forms of vegetable life. Acland remarks that "in seventeen of the British cases the individual infected had either been in the habit of chewing straws, ears of corn, &c., or had been engaged in agricultural pursuits." An analysis of the histories of the Middlesex series of cases is significant of a probable frequency of transmission of infection to man by various vegetable products. Of the seventy-eight individuals included in the series, twenty were either occupied with house-work or were "unoccupied," and in cases of eighteen others the occupation, if any, was not ascertained. Of the remaining forty, two belonged to the professional class, and thirty-eight to the working classes. Of the first two, one was a medical practitioner, and the other was a woman medical student who died as the result of appendix infection some months after taking a long summer holiday in the country. During her stay in the country the patient passed every day through a cornfield, and was in the habit of picking grains and chewing them.

Of the thirty-eight patients of the working classes, no fewer than twenty-four were engaged in occupations which brought them into close contact with vegetable products of one kind or another. The series includes: Coachmen and stablemen, seven; gardeners, three; bakers, two; foreman of timber-yard, one; carpenter, one; greengrocer, one; dairymaid, one; cellarman, one; working tailor or tailoress, seven.

The group of seven working tailors or tailoresses (the latter including two dressmakers) is an interesting one in this particular connexion; it includes two male and five female patients who would have been in the habit of constantly passing cotton between their lips. Of these, the two tailors had each a submaxillary abscess; the three tailoresses suffered respectively from pulmonary streptotrichosis, acute parotid abscess, and

a submaxillary abscess ; one dressmaker had a submaxillary abscess, and the other died with suppurative thrombosis of the superior mesenteric, splenic, and portal veins, resulting from appendix infection. Of the remaining fourteen patients of the working classes, one was a young man who lodged in a room over a stable, and another was a working blacksmith and farrier whose occupation would bring him into close contact with horses.

Comparison as to site of primary infection in the series of Middlesex Hospital cases with that in series of cases collected elsewhere is complicated somewhat, except for the pulmonary cases, by the fact that the former series comprises mostly cases of early infection in which an operation had been performed, or in which the patient had come under medical treatment for an acute illness, and in which the nature of the infection was established as a rule in the routine of every-day laboratory work. The series of collected cases, on the other hand, appear to be made up mainly of advanced cases in which either there was extensive disease of the lungs or secondary infection of the skin, or in which the nature of the disease was ascertained only after death. And in such advanced cases there would often be multiplicity of infective lesions, and consequent doubt or difficulty in determining the site of primary infection. On comparing the respective statistics, however, it is apparent that this difficulty of comparison arises chiefly in connexion with the published cases of "abdominal" infection. The proportion of early appendix cases at the Middlesex Hospital corresponds nearly with that of the more advanced cases of "abdominal" infection published from elsewhere. The site of primary infection was ascertainable definitely in most of the Middlesex cases. The only cases amongst the seventy-eight with regard to which there could have been any reasonable doubt in this matter were the following: There were five cases of right iliac abscess in which the appendix was not absolutely proved to have been the site of primary infection—these cases appear amongst the twenty cases of appendix infection. Then there was one case of renal streptotrichosis in which there was a history of chronic pulmonary trouble some two years previously, and in which it appeared likely that the lung had been the seat of original infection ; and there was a case, included with the cases of pulmonary streptotrichosis, in which the lung infection was of limited extent, in which there was a history of an operation for appendicitis eighteen months previously, and in which death, which occurred soon after the patient came into hospital, was apparently caused by some more serious intra-abdominal complication.

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Also there was a single case of streptotrichial cystitis, occurring in a stable-worker, in which it was probable that there were other undetected infective foci.

The following figures show, subject to what has just been stated, the site of primary infection in the seventy-eight Middlesex cases, in Acland's series of British cases, and in a larger series of 632 published cases collected by Rührah.

#### MIDDLESEX HOSPITAL CASES (78).

|   | Number of cases | Percentage |
|---|-----------------|------------|
| Infections of parts about the mouth and neck ... ..   | 40              | 51.2       |
| Appendix infections ... ..  | 20              | 25.6       |
| Pulmonary infections ... ..   | 14              | 18.1       |
| Other cases (conjunctivitis, renal streptotrichosis, cystitis, and case of accidental infection during an abdominal operation) ... .. | 4               | 5.1        |

#### ACLAND'S 109 COLLECTED BRITISH CASES.

|  |    |      |
|--|----|------|
| Infections of mouth, face, and neck ... ..   | 40 | 38.5 |
| Abdominal infections ... ..  | 42 | 38.5 |
| "Chest" infections ... ..  | 20 | 18.4 |
| Other cases (disease of testicle, of bladder, of prostate and rectum, of brain, and of orbit and brain) ... .. | 5  | 4.6  |

#### RÜHRAH'S 632 COLLECTED CASES.

|  |     |      |
|--|-----|------|
| Head and neck ... ..   | 359 | 57.0 |
| Digestive tract and abdominal organs ... ..                                | 132 | 21.0 |
| Thoracic viscera ... ..  | 92  | 14.5 |
| Other cases (infection of skin, 16; seat of infection doubtful, 33) ... .. | 49  | 7.5  |

From the foregoing considerations, then, it would appear that the Middlesex Hospital series of cases is not exceptional, and the apparently large number of cases found is due to the detection of early cases of mouth and appendix infections.

When considering the mortality amongst the Middlesex Hospital cases, the fact of early operation, and consequent discovery of the nature of the infection, must be kept in mind. Amongst the forty cases of infection of parts about the mouth only a single death is known to have occurred. In this case an abscess in the parotid region broke externally, and caused a progressive infection of the subcutaneous tissue of the right side of the neck and thorax; death resulted from lung complications. None of the other thirty-nine patients died whilst attending the hospital; most of the cases presented single and comparatively small abscesses in the cheek, or neck, or about the fang of a tooth. In some

of the cases, however, there was progressive infection of the subcutaneous tissue of the neck ; but in most the suppuration remained localized.

Amongst the twenty cases of appendix infection there were six deaths. In one case infection of the retroperitoneal tissue with prolonged suppuration occurred, and death happened about six months after the operation. In another case jaundice appeared ten days after operation, and death occurred sixteen days later, with suppurative thrombosis of the superior mesenteric, splenic, and portal veins. In a third case death followed a suppurative thrombosis of the portal vein some seven weeks after an operation ; in the last two cases the streptothrix was present in large quantities in the veins. In a fourth case death occurred twenty-two days after operation, again with thrombosis of the portal vein. In the other two fatal cases there was no examination after death, the exact cause of which remained uncertain. The remaining fourteen patients were discharged from hospital as either cured or improved. The only after-history obtained was in a case which had been discharged as apparently cured, but which came back to the hospital some months later with a sinus discharging pus, from which the streptothrix was again isolated.

Of the fourteen cases of lung infection, nine are known to have died, two were sent from the hospital to workhouse infirmaries in a hopeless condition, and the result in one case is not known. Of the two remaining cases of lung infection, one is believed to have been cured ; and in the other the progress of the disease appeared to have been, at any rate, arrested.

The cured case was that of a young girl, who was admitted under the care of Sir Alfred Pearce Gould, with an abscess in the upper part of the left breast. On incising the abscess a quantity of pus, with a pronounced faecal odour, was evacuated, and a streptothrix was obtained in pure culture. There were no physical signs of disease of the lung : but, in view of the finding, a further exploratory operation was carried out, and a sinus was found leading through an intercostal space into a small cavity in the underlying lung. This was dealt with, but a discharging sinus remained for more than a year, and ultimately healed with apparent complete recovery under treatment with large doses of iodide of potassium.

The other case was that of a stable foreman who came under the care of Dr. H. Campbell Thomson with an attack of hæmoptysis. The patient presented an excavated ulcer on the dorsum of the tongue ; and there was an area of deep-seated dullness towards the front of the upper



lobe of the left lung. A small opaque patch was located by radiography in the position indicated by the area of lung dullness, but otherwise there were not any signs of lung disease. Repeated scraping of the ulcer of the tongue failed to afford any evidence of streptothrix infection, but the sputum contained large quantities of a streptothrix parasite which was obtained in culture on several occasions. A vaccine was prepared from the streptothrix, and the specific treatment was carried out for many months. The patient's general condition improved, and as later he appeared to be perfectly well, the vaccine treatment was discontinued. All evidence of presence of the parasite had disappeared from the sputum; but apparently there was still a small indefinite area of dullness in the lung.

Of the remaining cases on the list, the only one which is known to have proved fatal was one in which there was accidental infection of the peritoneum in the course of an operation for appendicostomy, carried out for feeding purposes in a patient with an annular malignant stricture of the œsophagus. The patient died twenty-four days after the operation, and at the subsequent examination a condition of the peritoneum exactly resembling a miliary tuberculosis was found, with a dense aggregation of tubercles round the site of the implanted appendix. An acid-fast species—*Streptothrix eppingeri*—was isolated in pure culture from a number of the tubercles. This particular species has been identified by others in five published cases, and the circumstances under which infection occurred in one of these cases were curiously similar to those just mentioned. The case is one recorded by McCallum in the United States; the patient was a child on whom an operation of gastrostomy had been performed for a non-malignant stricture of the œsophagus. In this case death occurred twenty-three days after the operation, and a similar condition of the peritoneum was found. It seems to be clear that in each case there was an accidental infection of the peritoneum at the time of the operation—a consideration which suggests that the organism in question may be widely distributed in the air or in dust.

As to method of pathogenic action, it would appear that two distinct classes of parasites may be recognized, and that the pathogenic action of each class may be differentiated on broad lines. I have pointed out that the streptotrichæ may be differentiated roughly, from the laboratory point of view, into two classes according to the character of their growth on artificial media. There is what may be termed the saprophytic type of streptothrix, which grows freely on artificial media,

which presents the typical life-cycle when so growing, and which has in culture the typical appearance, and often the characteristic smell, of a mould. Judging from what one knows of the history of cases of comparatively early infection, streptotrichæ of this kind do not produce any very active toxins. They are injurious because of a progressive destruction of tissue, and in that they, and especially when infecting the lung, prepare the way for secondary infection by pyogenic organisms which form active toxins. The progress of an infection by a parasite of this class is such as is generally recognized as being characteristic of streptothrix infections. That is to say, the progress of infection proceeds either through contiguous tissues or by direct continuity of tissues. This method of pathogenic action was obvious in many of the cases which have been under observation at the Middlesex Hospital. An abscess in the substance of the cheek will first make its way to the surface, and then the parasite will track slowly and continuously down the subcutaneous tissue of the neck without, as a rule, extending to deeper parts. Similarly, with a lung infection the parasite will spread by continuity of tissue until it has reached the pleural surface of the lung. The two surfaces of the pleural sac then become adherent; the parasite grows across the adherent surfaces, and through an intercostal space. Having established itself in the subcutaneous tissue, the streptothrix next invades the plane of subcutaneous connective tissue, as in the case of the mouth infection. In one of the cases of the Middlesex series, the parasite, having perforated a left intercostal space in front, spread downwards on the left side of the body as low as the umbilicus, and upwards and backwards over the shoulder, then downwards to the level of the lower angle of the left scapula. In most cases apparently the skin itself is directly infected only in a slight degree, except that it is punctuated here and there by small ulcers which mark the sites of discharge of small abscesses which have formed in the subcutaneous tissue. Except for this the skin is not directly affected; its commonly observed dusky appearance in these cases is secondary to changes in the subcutaneous tissue. There is, as a rule, no spreading surface ulceration such as might be expected of skin infection. And consequently, in cured cases of the kind, the cicatricial contraction is of the subcutaneous tissue, and not of the skin itself. This tendency to subcutaneous spread of infection is noticeable in other mycoses. In experimental sporotrichosis, for instance, a subcutaneous inoculation of the special parasite is followed by a slow and progressive infection of the subcutaneous connective tissue, with little tendency to extension either to the epidermis above or to deeper

tracts of tissue until the late stages of the infection. In infections by this class of streptotricheæ—and apparently a large number of cases of appendix infection and of pulmonary streptotrichosis are thus caused—there is at first but little tendency to diffusion of infection by means of either the blood or the lymph-stream. It is only in far-advanced cases of infection by this class of organism that secondary infection of parts remote from the site of primary infection is frequent. And, in view of the apparent frequency of liver infection, as set out in the notes of published cases, it would appear to be probable that such liver infection is often a result of invasion of the tributary veins of the portal system in cases of appendicitis by direct extension of the growth of the parasite through the walls of the vessels.

With regard to the second class of streptotricheæ, we have now to consider the method of action of a different kind of pathogenic parasite. We have to consider the action of parasites which may be rapidly disseminated through the tissues by the lymph or blood-stream. And, as the second class of parasites differ from the other class in their method of pathogenic action, so they are usually differentiated from the others also by their biological characteristics. With them the "mould" type is less strongly pronounced; and the species are, as a rule, difficult and uncertain of growth on artificial media. Also, under the conditions of culture on artificial media these organisms are likely to be mistaken for pleomorphic bacilli. The now recognized *Streptothrix lepræ* may be taken as a type of this class of streptotricheæ; and Koch's *Bacillus tuberculosis* is believed by some of us to occupy a like position.

But apart from cases recognized as cases of tuberculosis or as cases of leprosy, a considerable number of cases of generalized infection by streptotricheæ of the type referred to have been recorded; and it appears probable that other cases of the kind may not infrequently be mistaken for cases of tuberculosis. The difficulty arises from two sources. In the first place, the lesions occurring in this kind of infection may be indistinguishable anatomically from lesions which are commonly believed to be characteristic of infection by Koch's bacillus; and, in the second place, the identification by laboratory methods of the true nature of the causative parasite is often a matter of extreme difficulty. Not only are streptotricheæ of this class frequently difficult of growth on artificial media but often the mycelial form of the organism is rapidly transient. Fragmentation of the mycelium and sporulation occur very rapidly, and so the true mycelial characteristics of the organism escape observation. Several species of streptotricheæ of this type are acid-fast when stained

by the Ziehl-Neelsen method; and whether by the anatomical features of the lesions which they cause or by their morphology when growing on artificial media, are practically indistinguishable from Koch's *Bacillus tuberculosis*. So far as we know, the differentiation for practical purposes can be arrived at only by observation of the character of the growth on artificial media—which growth is, as already stated, often difficult to obtain—and, in some cases, by difference in pathogenic action for inoculated animals.

With regard to the ordinary paths of infection of pathogenic streptotricheæ, it would appear that in many cases the infection originates in the growth of the parasite along a natural duct, with subsequent invasion of contiguous parts. This method of establishment appears to be the rule in cases of infection of parts about the mouth, and in cases of streptotrichial appendicitis. In the former group of infections the occasional establishment of a streptothrix in the tissues by entry along sinuses or passages connected with carious teeth is also certain from clinical observation. In the case of mouth infections, passage of the parasite along the ducts of the salivary glands is suggested by the frequency of abscesses along the course of the duct of the parotid gland and in the situation of the gland itself. Attention has been specially called to this point by Mr. T. Kellock; and the frequency of streptotrichial abscess in the situation of the submaxillary and sublingual glands is also strongly suggestive of this route of infection. In one case, under the care of Mr. Somerville Hastings, at the Middlesex Hospital, there was an abscess in the cheek which was situated along the course of the parotid duct, and pressure along the duct caused the discharge of drops of pus, from which the parasite was obtained in pure culture. In other cases of mouth infection, and especially in lesions on the dorsum of the tongue which occur occasionally in man and which are common in cattle, the parasite enters the tissue through accidental abrasions of the mucous membrane, which in cattle are probably caused by the temporary lodgment of ears of infected grain. The crypts of the tonsil also afford opportunity for the establishment of the parasite in both man and cattle. Pulmonary infection appears to result, as in the case of chronic pulmonary tuberculosis, from the inhalation of infected dust; and the special liability to infection of those who habitually inhale dust derived from vegetable products has been referred to. No comment is necessary on the considerable proportion of cases of early infection of the canal of the appendix cæci which is shown in the Middlesex Hospital series. Another possible route of infection is to the liver by the common

bile-duct; but it is probable that in a large number of advanced cases, with multiplicity of lesions, the liver has been regarded as the original seat of infection when the primary infection was really of the appendix, with secondary infection of the liver by the portal vein route.

The last point which has to be mentioned is the difficulty of accurate diagnosis in these cases. In very many cases an exact diagnosis on clinical evidence is impossible. After one has excepted cases in which the occurrence of an abscess about the mouth raises suspicion of a possible streptotrichial infection and advanced cases in which there has been a progressive infection of the subcutaneous tissue with characteristic appearances on the surface, there are no means for the differentiation clinically of streptotrichoses from many other kinds of infection. In pulmonary infections the clinical symptoms and signs are those of chronic phthisis; and it is only the occasional perforation of an intercostal space, with possibly subcutaneous extension of the infection, which may help in differentiating a case from one of pulmonary infection by Koch's parasite. In the latter infection, however, perforation of the chest wall is probably of extremely rare occurrence. And it may be added that in only one of the fourteen cases of pulmonary streptotrichosis examined at the hospital was there any suggestion that the disease was other than an ordinary tuberculous phthisis, until suspicion was raised by failure to find typical "tubercle bacilli" in the sputum, or until typical mycelial forms of a non-acid-fast streptothrix had been identified in the sputum. Equally, a diagnosis by clinical methods of the specific kind of infection is impossible in acute streptotrichial infection of the appendix, or in any case unless there has been extension to the subcutaneous tissue. In the case of mouth infections, whilst there is nothing characteristic about the local abscesses which form in the cheek or neck, the situation of the swelling, and sometimes the occupation of the patient, may suggest a diagnosis.

And whilst clinical diagnosis as to the special kind of infection is impossible in the majority of cases of streptotrichosis, the difficulties in the way of the positive identification of the parasite by laboratory methods are frequently considerable. These difficulties arise from two sources: in the first place there is the extreme difficulty of obtaining growth of many parasites of this class on artificial media, and in the second place there is the difficulty arising out of the varying morphology of these species of moulds at different phases of their life-cycle. It is now well recognized that the mycelial, or "ray fungus" form, represents only one

of the three forms under which these parasites occur; and this typical mycelium, and the mycelium when in the earlier stages of "fragmentation" it is breaking up into "rod forms," represent the only stage at which the parasite can be recognized positively by microscopic examination. At a later stage of development, when fragmentation of the mycelium is complete, and when sporulation has occurred, the picture is no longer that of a "ray fungus"—all that can be seen in a stained film is a collection of somewhat irregular "bacillary" forms, and spherical spores which exactly resemble the common pus cocci; and both forms stain deeply with Gram's method. The difficulty in practice may be illustrated by reference to what is often found on examination of the exudation in cases of appendicitis. A film stained by Gram's method shows a dense collection of deeply stained spherical and rod forms, together with, or without, bacillary forms which do not stain by Gram's method and which probably prove on culture to be *Bacillus coli communis*. But in a quite large proportion of such cases growth of either of the Gram-stained organisms cannot be obtained. This failure to obtain growth is, in itself, a reason for suspecting that the spherical forms do not represent cocci, since none of the known Gram-staining pathogenic cocci are difficult of growth on artificial media. Suspicion will be increased by the presence of largish masses of minute Gram-staining particles, which probably represent the débris of degenerated masses of mycelium. But these appearances merely give rise to suspicion; positive identification such as is necessary for statistical purposes is impossible unless definite, branched, mycelial filaments which stain by Gram's method are found, or unless the identity of the parasite is established by culture. And it is for this reason that I believe that cases of infection by streptotrichææ are very frequently overlooked; and that is why it appears probable that our own statistics at the Middlesex Hospital understate the frequency of the occurrence of streptotrichoses.

In the case of the acid-fast species the difficulty, without successful culture, is still greater, since their appearance as they occur in morbid material may be identical with that of either branching or plain rod forms of the variety of strains, or species, recognized under the name of *Bacillus tuberculosis*—a difficulty which is readily explainable if it is true that what is ordinarily recognized in clinical practice as tuberculosis includes, in fact, one or more specific varieties of streptotrichosis. The difficulty, and in this particular case its solution, may be illustrated by a comparison of one well-defined species, *Streptothrix eppingeri*, with the common strain of Koch's bacillus. The lesions, those of a grey miliary



tuberculosis, produced by either may be identical, both to the naked eye and histologically under microscopic examination. Both micro-organisms stain by Gram's method; both acquire acid-fast staining properties with age, but *Bacillus tuberculosis* earlier and more extensively than the other. But the growth of Eppinger's streptothrix on artificial media is much more rapid than that of the tubercle bacillus, and is of quite different appearance; moreover, its pathogenicity for the rabbit is very much more active—death, with a widespread peritoneal tuberculosis, following within a few days of an intraperitoneal injection.

#### DISCUSSION.

Mr. ARTHUR BARKER said his own personal experience of cases of actinomycosis was comparatively limited, but Mr. Williams, the Registrar of University College Hospital, had made a collection of cases, and was present to give the figures. He (the speaker) had only had about half a dozen such cases in the hospital. The first he remembered involved the neck, with the usual glandular enlargement breaking down, in the person of a Lincolnshire farmer. That occurred years ago, when the knowledge of the disease was but slight. The next case was in the muscular abdominal wall, and all who saw that case suspected it to be sarcoma. At the excision he came upon a cavity full of the characteristic yellowish-green material, with the rosettes of actinomycosis. The next case was in the cæcal region, and was mistaken by him for a case of ordinary appendix abscess. But the drainage required was long, and in the end its true nature was recognized. Extension occurred throughout the abdomen, and the patient died of exhaustion. Another puzzling case which he was asked to see in the medical ward was that in which there was a large swelling in the lumbar region, with intense pain and high temperature, but with only a very moderate amount of breaking down. That extended, and death was from general exhaustion. The next case also was in the right flank; it passed from his hands during the vacation, but his colleague Mr. Trotter, he understood, did a rather extensive operation, which was successful. In another there was a large abscess in the cæcal region, which he opened, and the patient was still in the house, doing well under injections of iodipin. The only comment he would make upon it was, that after three operations, opening abscesses in various parts of the abdomen, the last on the left side, the patient was extremely exhausted and wasted, and after opening it was suggested that iodipin should be injected



into all the sinuses. This was done some months ago, and the patient had improved enormously; she was fat, up and about, and the sinuses seemed inclined to heal. He had not yet given iodide of potassium. The last case had some bearing on the remarks of Dr. Lovell. It was that of a gentleman who was sent to him by Mr. J. H. Badcock, with a ready-made diagnosis of actinomycosis. The patient had consulted Mr. Badcock about a loose tooth. This he extracted, and was struck by the peculiar material which surrounded the fang. He scraped it and sent it to Mr. Barker in a bottle. Dr. Thiele, the pathologist to the hospital, examined it and found actinomycotic material in it. He (Mr. Barker) thought a radical operation in that case most desirable, though he might be influenced in regard to a future case by what Dr. Lovell had said. He cut into the jaw on either side, about  $\frac{1}{2}$  in. from the infected socket, and took out the piece, and he excised the submaxillary glands there and then. That was about three years ago, and the patient had remained well in the interval. Whether it would have been better to trust to iodide of potassium in that case he did not know, but he believed what he did was on the safe side. Those were the only cases of the condition which he remembered to have had under his own care.

Mr. GWYNNE WILLIAMS said that for the purposes of a paper read before the Medical Society at University College Hospital he had collected cases of ileo-cæcal actinomycosis which were admitted to the hospital in the last four years. There were six cases, which he thought must be attributed to the appendix. Such cases came into three definite classes. The first group was the commonest, and there were three instances of that—namely, that of acute appendicitis. They were operated upon, and a culture was made in the ordinary way, but nothing grew. In one there was considerable peritonitis, and in the other there were localized abscesses. Two of them healed up without trouble, but came again later with residual abscesses in the mid-line of the abdomen. Those abscesses had the characteristic signs of actinomycosis—i.e., considerable infiltration, and where the abscess came to the surface there seemed to be much pus, which when opened showed a very small abscess cavity. One of Mr. Barker's cases, in which there was considerable peritonitis, was closed at the operation, but it broke down afterwards. It was not until some time later, drainage being prolonged, that the true nature was discovered. The next class was that in which there was a tumour in the ileo-cæcal region. There was

one case of this class. The patient was a man aged 45, a tinsmith, from the country, who had had pain nine months. There were no signs of obstruction, and there had been no blood or slime in the stools. In the right iliac fossa there was a definite lump, fixed to the posterior abdominal wall. It was explored by Mr. Trotter, who at the time rather suspected actinomycosis, because of the density of the surrounding tissue. When the appendix was removed, its walls were found to be thickened, apparently from chronic inflammation. There was no ulceration of mucous membrane, but there was a fibrotic mass in the wall along the line of its mesentery. A considerable part of the iliacus was removed, and the specimen showed what was characteristic of actinomycosis—namely, a spread from the appendix to the iliacus and to the wall of the cæcum, but not affecting the mucous membrane of the latter. Of the next class there were two, and a specimen of such a case was now on exhibition. This class showed the extensive infiltration of the cellular planes. One man came with his thigh flexed almost to a right angle, and he had a very dense swelling in the right iliac fossa. It was opened by Sir Rickman Godlee, and the pus was found to contain actinomycosis. It had spread into the posterior abdominal wall, and caused contraction of the psoas. Another case was that of a man who came with sinuses down to the front of the thigh, from which actinomycotic nodules were obtained; here the infection had spread into the connective tissue. There was another case, mentioned by Mr. Barker, in which the patient came complaining of pain in the right loin. For a considerable time this was believed to be a renal case, but there was only a trace of pus in the urine, and no stone was revealed by the skiagram. A swelling developed which projected into the right loin. Mr. Barker opened it, and a small quantity of pus came away. No culture grew in the tube. Subsequently it was explored by Mr. Trotter: it showed the characteristic induration of actinomycosis and the sinus bled very freely. The patient was explored later by Mr. Barker, and at the operation the tip of the appendix was found buried in the mass on the posterior abdominal wall. Subsequently the patient died. He felt sure it was an appendix infection from the first.

The PRESIDENT (Mr. G. H. Makins, C.B.) said he thought some of the points which had been raised in connexion with this subject were worthy of a little more discussion. One of them concerned the manner in which this disease was acquired. Mr. Foulerton had been at some pains to show that a large number of the cases which he had examined

had occurred in people who handled straw or grain. Most members probably believed this, but Mr. Kellock's remarks tended to show that the disease might occur in people of any occupation. In the few cases which were dealt with at St. Thomas's Hospital he noted what were the occupations. One was a miller's carman, one an agricultural labourer, and another was a horse-keeper. On the other hand, one was an insurance collector, one a policeman, another a plasterer, and others a tube railway gateman and a news vendor. Of course, it might be said that everyone occasionally unpacked a case packed with straw, and thus ran some slight risk of infection. It seemed that there must be some more ready way of acquiring the disease than from habitual contact with straw or grain. He could not remember the reference, but some time ago he was interested in reading an account of some cultivations made from the interior of eggs which had been packed in straw, and which yielded this streptothrix. That suggested a way in which the disease might be distributed among an urban population. And there must be other articles of food which conveyed the disease. Another point of interest was the mortality of the disease. Every patient he had seen with abdominal or pulmonary actinomycosis had died, and within a year of first coming under observation. After what Mr. Foulerton said, it seemed clear that these cases had not been diagnosed at an early enough date. Apparently the diagnosis in the Middlesex Hospital cases of actinomycotic appendicitis was made after the operation had been done, suspicion arising from the appearance of the appendix. The disease, therefore, was in an earlier stage than the speaker had met with, which made an immense difference, as in all the cases he had seen it was impossible to eradicate the condition. There had not been much said as to treatment, but both Mr. Foulerton and Dr. Lovell referred to the question of vaccines. He had seen patients improve on large doses of iodide of potassium, but it had absolutely failed to do real good in cases of extensive involvement, probably because of the existence of secondary infection. The only other drug he had tried was sulphate of copper, as recommended by Dr. Bevan, but he could not say that he had seen any marked effect from this, given either internally or used as a solution for local application. Sulphate of copper was perhaps useful as an alternative when iodide of potassium had been given for some time. The Section would feel particularly indebted to Mr. Foulerton for what he had said and shown on the screen, which explained the difficulties in which the pathologist found himself, and the reason why the surgeon might be disappointed when he came to the pathologist for aid.

Mr. JAMES BERRY considered that two points of considerable interest had emerged from the papers and discussion. One of them the President had alluded to—namely, the proclivity of the disease, when affecting the deeper parts, to end fatally. The other point he would touch on was the frequent difficulty of the diagnosis from the microscopic point of view, even in the hands of skilled pathologists. He thought that the true nature of the case was for this reason often overlooked in that early stage when alone cure by operation was likely. Some years ago he had seen, with Dr. Square, of Leighton Buzzard, a young man, clerk in a corn-chandler's office. He had a small mass of enlarged glands near the angle of the jaw which were at first thought to be tuberculous; but the glands were very hard, and somewhat attached to the skin, and there was a small sinus over them, discharging a few drops of pus which looked peculiar, and which, although not yellow, nevertheless showed under the microscope typical actinomycosis mycelium. He proceeded to the removal of the area affected, and found he had embarked on an extensive procedure, as he had to clear out most of the anterior triangle, and expose the carotid and jugular veins for several inches. It was one of the most extensive operations he had ever done on the glands of the neck. The patient made an excellent recovery, and when seen again, several years later, was still in excellent health, with no recurrence. He did not doubt that if the case had been allowed, before resorting to operation, to progress until there was extensive glandular enlargement, the patient would have succumbed to the disease. He was surprised to hear Dr. Lovell say he thought the surgeon should not intervene in the early stage. His own feeling was that most cases were seen by the surgeon at a stage when the disease had already progressed too far for surgery to be of much use. When the thorax, cæcum, spleen, &c., were involved, one could scarcely hope to remove the disease by operation, and it was often better not to operate at all. But when a small and accessible area only was involved, it was often better to do an extensive operation, though he would have no objection to trying the effect of iodide of potassium for a short time. When the disease had progressed to any considerable extent, mere scraping operations were of very little use, and might leave the patient worse instead of better.

Dr. LOVELL, in reply, said he thought the question of treatment would resolve itself into finding out more about the disease, so that the diagnosis could be made with certainty before the incision was performed. He suggested that one possible method of recognition was the agglutina-

tion reaction. He knew cases in which that was positive, but the test had only been applied after operation. If this could be done earlier, surgery in some cases might be averted. There was a time when tubercular lesions were dealt with more drastically than now, and a similar change might come about in the case of actinomycosis. Medical means were especially desirable where the lesion was about the face. With regard to grain being the carrier of the disease, he had been told there was a great prevalence of actinomycosis in the south of France, where cases were frequent in people who fed pigeons with grain which they had previously chewed.

Mr. FOULERTON, in reply, said that he thought that the disease occurring in the persons (*gaveurs*) who fed Bordeaux pigeons in the way mentioned by Dr. Lovell was usually an aspergillosis, and not a streptotrichosis. Also the egg infection in farms in the south of France was apparently an aspergillosis usually. Most of the cases of infection of parts about the head and neck which were included in his paper had been under the treatment of either Mr. Murray or Mr. Kellock at the Middlesex Hospital, and had been operated on early. The only known fatal case in the series of mouth infections was that of a man who did not come under hospital treatment until infection had tracked from the region of the parotid down to the pectoral region. In early cases of streptothrix infection of the appendix, which could not be diagnosed as such before operation and bacteriological examination, an operation would free the patient of the disease. But when the infection had spread, by the time of operation, from the appendix to the retro-peritoneal connective tissue, operative interference would not be effective. With regard to lung infections, of the fourteen cases on his list, eleven were certainly dead and another was probably dead: of the survivors, one had been treated with iodide of potassium, and one with a vaccine. So far as he knew, there were only two or three published cases in which a vaccine had been used, apart from the two cases mentioned in the discussion, and there was not sufficient material on which to estimate the value of the treatment. At any rate, the Middlesex Hospital experience went to show that when surgical treatment was possible in streptothrix infections it should be carried into effect at the earliest opportunity. He had not intended to suggest that in every case of streptotrichosis the infection was derived from grain or grasses, but experience had shown that a high proportion of such infection occurred amongst those whose occupation brought them into constant contact with grain or grasses.

**Statistics of Actinomycosis, 1902-1912.***From Charing Cross Hospital.*

By A. E. MORTIMER WOOLF, F.R.C.S.

1903: Glands of neck.

1909: Appendix. Appendix abscess opened two years previously. Sinus persisted. Appendix found to communicate with abscess cavity in which actinomycosis was discovered. Also glands of neck in another case.

1910: Abdominal wall and subcutaneous tissues in front of sternum. Died of a cerebral abscess in which no actinomycosis was found.

1911: Abdominal wall—scraped. Eventually died in a convalescent home.

In the Museum there are three specimens of the disease, all of the liver (Nos. 1,266, 1,266A, and 1,266B).

*From St. George's Hospital.*

By C. H. S. FRANKAU, F.R.C.S.

|                         |     |     |     |     |     |     |     |    |
|-------------------------|-----|-----|-----|-----|-----|-----|-----|----|
| Lower jaw               | ... | ... | ... | ... | ... | ... | ... | 4  |
| "Mouth "                | ... | ... | ... | ... | ... | ... | ... | 1  |
| Over malar bone         | ... | ... | ... | ... | ... | ... | ... | 1  |
| In temporal region      | ... | ... | ... | ... | ... | ... | ... | 1  |
| Of cheek                | ... | ... | ... | ... | ... | ... | ... | 2  |
| Of neck                 | ... | ... | ... | ... | ... | ... | ... | 1  |
| Of face                 | ... | ... | ... | ... | ... | ... | ... | 2  |
| Of chest wall and thigh | ... | ... | ... | ... | ... | ... | ... | 1  |
| Abdominal               | ... | ... | ... | ... | ... | ... | ... | 6* |
| Liver                   | ... | ... | ... | ... | ... | ... | ... | 1  |

\* Fallopian tubes, 1; appendix, 1; unknown origin, 4.

*From the Middlesex Hospital.*

By E. PEARCE GOULD, B.Ch.

|                            |     |     |     |     |     |     |    |
|----------------------------|-----|-----|-----|-----|-----|-----|----|
| Mouth, neck and face       | ... | ... | ... | ... | ... | ... | 96 |
| Appendix                   | ... | ... | ... | ... | ... | ... | 13 |
| Iliac abscess (? appendix) | ... | ... | ... | ... | ... | ... | 4  |
| Peritonitis                | ... | ... | ... | ... | ... | ... | 2  |
| Empyema                    | ... | ... | ... | ... | ... | ... | 2  |
| Renal                      | ... | ... | ... | ... | ... | ... | 1  |
| Palm of hand               | ... | ... | ... | ... | ... | ... | 1  |
| Pus (? source)             | ... | ... | ... | ... | ... | ... | 2  |
| Total                      | ... | ... | ... | ... | ... | ... | 61 |

*From the London Hospital.*

By H. S. SOUTTAR, M.Ch.

|      |     |         |     |                               |     |     |      |
|------|-----|---------|-----|-------------------------------|-----|-----|------|
| 1904 | ... | Female  | ... | Skin of face                  | ... | ... | —    |
| 1905 | ... | Male    | ... | Jaw                           | ... | ... | Died |
| 1906 | ... | Female  | ... | Jaw                           | ... | ... | —    |
| 1907 | ... | *Male   | ... | Liver, lumbar spine, meninges | ... | ... | Died |
| 1910 | ... | Female  | ... | Chest wall (followed empyema) | ... | ... | —    |
|      |     | Female  | ... | Lower jaw                     | ... | ... | —    |
|      |     | Male    | ... | Neck                          | ... | ... | —    |
|      |     | Male    | ... | Abdominal wall                | ... | ... | —    |
| 1911 | ... | Male    | ... | Lip                           | ... | ... | —    |
|      |     | Male    | ... | Colon                         | ... | ... | —    |
| 1912 | ... | *Male   | ... | Appendix                      | ... | ... | Died |
|      |     | *Male   | ... | Peritoneum and liver          | ... | ... | Died |
|      |     | *Female | ... | Appendix                      | ... | ... | Died |
|      |     | *Female | ... | Appendix                      | ... | ... | Died |

We have pathological specimens of the cases marked \*.

*From St. Bartholomew's Hospital.*

By H. W. WILSON, F.R.C.S.

|      |     |          |                                |     |     |           |
|------|-----|----------|--------------------------------|-----|-----|-----------|
| 1902 | ... | 1        | Actinomycosis of liver         | ... | ... | Recovered |
|      |     | 2        | " abdominal wall               | ... | ... | Died      |
|      |     | 3        | " appendix                     | ... | ... | Recovered |
|      |     | 4        | " iliac fossa                  | ... | ... | Recovered |
| 1903 | ... | 5        | " chest wall, pericardium, &c. | ... | ... | Died      |
| 1904 | ... | 6        | " abdominal wall               | ... | ... | Died      |
|      |     | 7        | " abdominal wall               | ... | ... | Recovered |
|      |     | 8        | " jaw                          | ... | ... | Recovered |
| 1905 | ... | 9        | " face and neck                | ... | ... | Recovered |
|      |     | 10       | " face and neck                | ... | ... | Recovered |
| 1906 | ... | 11       | " breast                       | ... | ... | Recovered |
| 1907 | ... | 12       | " abdominal wall               | ... | ... | Recovered |
|      |     | 13       | " appendix                     | ... | ... | Died      |
| 1908 | ... | No cases |                                |     |     |           |
| 1909 | ... | 14       | Actinomycosis of liver         | ... | ... | Died      |
|      |     | 15       | " caecum, abdominal wall, &c.  | ... | ... | Died      |
| 1910 | ... | 16       | " caecum                       | ... | ... | Died      |
|      |     | 17       | " caecum                       | ... | ... | Died      |
|      |     | 18       | " intestine                    | ... | ... | Recovered |
| 1911 | ... | No cases |                                |     |     |           |

The best specimens in our Museum of this disease are:—

|                               |                         |                          |                                     |
|-------------------------------|-------------------------|--------------------------|-------------------------------------|
| Nos. 2,239A)<br>2,239E) Liver | No. 2,035C <sub>1</sub> | { Caecum and<br>appendix | Nos. 541a)<br>541b) Ox jaw<br>541c) |
|-------------------------------|-------------------------|--------------------------|-------------------------------------|



## From St. Thomas's Hospital.

By B. C. MAYBURY, B.S.

| No. | Case     | Sex | Age | Occupation            | Duration of history | Total duration of illness | Primary focus                  | Organs substantially affected               | Microscopical examination   | Blood count                              | Treatment   | Result | Remarks  |
|-----|----------|-----|-----|-----------------------|---------------------|---------------------------|--------------------------------|---|-----------------------------|--|---|--------|--|
| 1   | W. W.    | M.  | 46  | Insurance collector   | 3 months            | 34 months                 | Liver                          | Peritoneum                                  | Actinomyces                 | White cells, 8,000; F.G.O., 88 per cent. | Incision and drainage   | Died   | Death due to general peritonitis resulting from bursting of a retrocolic abscess |
| 2   | H. J. L. | M.  | 26  | Police constable      | 3 weeks             | 9 months                  | Right iliac fossa (? appendix) | Liver, both pleura, retroperitoneal tissues | Actinomyces                 | White cells, 13,000                      | Incision and drainage   | Died   | --   |
| 3   | D. C.    | M.  | 45  | Miller's carman       | 8 months            | 83 months                 | Liver                          | Chest wall                                  | Actinomyces (Gram-positive) | --                                       | Incision and drainage; potassium iodide up to 45 gr. per diem; no improvement         | Died   | --   |
| 4   | W. W.    | M.  | 42  | Agricultural labourer | 5 months            | --                        | Liver                          | Chest wall                                  | Streptothrix                | --                                       | Incision and drainage; potassium iodide up to 105 gr. per diem; temporary improvement | Died   | --   |

|    |          |    |    |                       |          |           |                                |  |              |   |  |      |   |
|----|----------|----|----|-----------------------|----------|-----------|--------------------------------|--|--------------|---|--|------|---|
| 5  | W. C.    | M. | 43 | Plasterer             | 9 months | 11 months | Right lung                     | Chest wall   | Actinomyces  | —   | Incision and drainage; potassium iodide up to 105 gr. per diem; no improvement   | Died | —   |
| 6  | E. M.    | M. | 45 | Horse-keeper          | 3 weeks  | 6 months  | Hypogastrium (? appendix)      | Liver, lungs (right and left), brain (3 abscesses) | Actinomyces  | White cells, 16,000                         | Incision and drainage; potassium iodide up to 36 gr. per diem; no improvement  | Died | —   |
| 7  | T. C.    | M. | 19 | Gateman, tube railway | 1 month  | 4 months  | Right lung                     | Chest wall, liver                                  | Streptothrix | White cells, 27,000                         | Incision and drainage; potassium iodide up to 120 gr. per diem; temporary improvement; copper sulphate, 4 gr. t.d.s.           | Died | Hydatid complement fixation test positive   |
| 8  | C. J.    | M. | 21 | Mirror maker          | 7 months | 13 months | Right iliac fossa (? appendix) | Liver  | Streptothrix | White cells, 14,780<br>F.G.O., 70 per cent. | Incision and drainage; potassium iodide up to 45 gr. per diem; some temporary improvement; liquor arsenicalis, 4 minims t.d.s. | Died | Died from hemorrhage from external iliac artery; miliary tubercles (due to <i>Bacillus tuberculosis</i> ) in spleen; both lungs |
| 9  | F. G. A. | M. | 37 | Newspaper vendor      | 3 months | —         | Right iliac fossa (? appendix) | Retroperitoneal tissues and muscles of loin        | Actinomyces  | —   | Incision and drainage; potassium iodide; appendicectomy; copper sulphate   | —    | —   |
| 10 | S. S.    | M. | 38 | Cab-driver            | 3 months | 3½ months | ? appendix                     | (? pelvic peritoneum); liver, right lung           | Actinomyces  | —   | Appendicectomy; later laparotomy   | Died | —   |

*From Guy's Hospital.*

By L. BROMLEY, F.R.C.S.

|       |     |     |   |                                    |     |                          |
|-------|-----|-----|---|------------------------------------|-----|--------------------------|
| 1911  | ... | ... | 0 | ...                                | ... | —                        |
| 1910  | ... | ... | 1 | ...                                | ... | Upper jaw and cheek      |
| 1909  | ... | ... | 0 | ...                                | ... | —                        |
| 1908  | ... | ... | 1 | ...                                | ... | Cheek                    |
| 1907* | ... | ... | 2 | ...                                | ... | (a) and (b) both cheek.  |
| 1906  | ... | ... | 0 | ...                                | ... | —                        |
| 1905  | ... | ... | 1 | ...                                | ... | Lower jaw                |
| 1904* | ... | ... | 1 | ..                                 | ... | Dorsum and side of foot  |
| 1903  | ... | ... | 0 | ...                                | ... | —                        |
| 1902  | ... | ... | 2 | ...                                | ... | (a) lower jaw; (b) cheek |
|       |     |     | 8 | (Check, 5; lower jaw, 2; foot, 1.) |     |                          |

\* Two cases in 1907, and one case in 1904, are queried: in none of these cases was the diagnosis confirmed by bacteriological examination.

## **Surgical Section.**

February 11, 1913.

Mr. G. H. MAKINS, C.B., President of the Section, in the Chair.

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### **The Cause and Treatment of certain Unfavourable After-effects of Gastro-enterostomy.**

By ARTHUR F. HERTZ, M.D.

As a result of modern improvements in technique, the unfavourable complications, which were formerly not infrequent after gastro-enterostomy, have become more and more rare. It must, however, have been the experience of almost every surgeon that patients, upon whom a gastro-enterostomy had been performed, have at some later period complained of symptoms, which were often trivial in comparison with those of the condition for which the operation was carried out, but which were none the less sufficient to prevent the patient from regarding the result of the operation as entirely satisfactory. In the last few years I have been consulted by a considerable number of such patients at intervals varying from a few weeks to several years after the operation, which had been performed for various conditions, but most commonly for duodenal ulcer. I have gradually come to recognize that the symptoms in a considerable proportion of the cases are due to a cause which has not hitherto been described, and in others are the result of a condition which has up to now only been incidentally referred to by Jonas [2] in 1908.

#### **(I) TOO RAPID DRAINAGE OF THE STOMACH.**

The patient complains of a sensation of fullness, which occurs during each meal, and which may be so unpleasant that the amount of food taken is progressively diminished, and a considerable loss of weight may

finally occur. The sensation disappears rapidly, and the patient may find that by eating with extreme slowness he is able to prevent its occurrence. Many patients recognize that this sense of fullness is localized slightly lower than the position where the pain or discomfort, for which the operation was performed, was felt.

In some cases the patient also complains of slight diarrhœa, the bowels being opened after each meal; the first stool passed in the day is generally solid, but the later ones are unformed and occasionally fluid. In rare cases the diarrhœa may be severe, and a case which has been reported of a patient dying from diarrhœa after gastro-enterostomy was probably of this nature, no organic cause having been discovered at the autopsy.

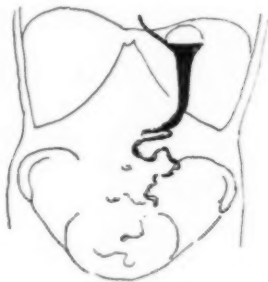


FIG. 1.

Five years after gastro-enterostomy for small duodenal ulcer, which did not produce obstruction.

In all patients suffering from this group of symptoms I have found with the X-rays that the stomach was small and hypertonic and that the passage of food out of it was extremely rapid, so that a meal, consisting of half a pint of porridge and milk mixed with 2 oz. of bismuth oxychloride or barium sulphate, left the stomach in less than an hour, and in one case a quarter of an hour after being taken, instead of requiring the normal three or four hours. If the patient is watched whilst he is taking the meal, the outflow from the stoma may indeed appear to be almost as rapid as the inflow from the œsophagus (fig. 1). In all cases, whether there was any pyloric obstruction or not at the time of the operation, little or nothing passed through the pylorus, and sometimes the chyme even failed to reach the portion of the pyloric end of the stomach beyond the stoma. The part of the jejunum into which

the gastric contents pass from the stoma is consequently distended in a way which never occurs normally, as the duodenum and end of the ileum are the only parts of the small intestine which are ever full under natural conditions. I believe this distension of the jejunum is the cause of the sense of fullness, as the experiments described in my Goulstonian Lectures proved that distension, which leads to stretching of the muscle-fibres, is the only adequate stimulus of visceral sensation. In confirmation of this, the situation of the sensation is found to be lower than that due to gastric distension, and corresponds to the upper limit of the situation of the pain felt when the small intestine is subjected to rapid distension. The patient sometimes finds that anything which increases the activity of the small intestine, such as exercise or a dose of castor-oil, though it may increase the discomfort, makes it disappear more rapidly than it would do otherwise, doubtless because the distension of the jejunum lasts for a shorter period.

Confusion with the symptoms arising from a jejunal or gastro-jejunal ulcer is prevented by the fact that the nature of the diet has a considerable influence on the latter, whereas in this type of post-operative indigestion the quantity and not the quality of the food is alone of importance.

The diarrhœa is mainly due to the irritation of the bowels by the food, which escapes from the stomach too rapidly for efficient gastric digestion; owing to the absence of the normal stimulation of pancreatic secretion by hydrochloric acid in the duodenum it does not undergo sufficient compensatory digestion in the intestine. It tends to occur after meals owing to the normal gastro-colic reflex, which I have shown leads to an increase in the peristalsis of the colon whenever food enters the stomach [1]. In all probability there is also an entero-colic reflex, which arises from distension of the jejunum and produces the same result.

Complete relief or considerable improvement occurs if the patient is instructed to lie down for half an hour or an hour after each meal, as it is found with the X-rays that the stomach empties itself much less rapidly when this posture is assumed, the stoma no longer being in the most dependent position. In some cases it is better to lie on the right or less frequently on the left side, the best position being easily ascertained by watching the rate of evacuation with the X-rays. The patient should also be given some active preparation of pancreatic ferments, such as pankreon, at each meal, in order to compensate for the deficiency of the normal secretions. If the sense of fullness is still

experienced in spite of the treatment I have described, small doses of belladonna, which causes the involuntary muscle-fibres of the intestines to relax, and of codeine, which diminishes the excitability of the visceral nervous system, should be given half an hour before meals.

If all treatment fails to give relief and the patient's symptoms are severe, it might perhaps be necessary to perform an operation with the object of diminishing the size of the stoma, or, if the pylorus is not obstructed, of restoring its activity by completely closing the stoma. The interesting question also arises whether surgeons have not gone somewhat too far in their desire to obtain sufficient drainage, and whether it would not be advisable in the future to make a somewhat smaller stoma than has commonly been made in the last few years.

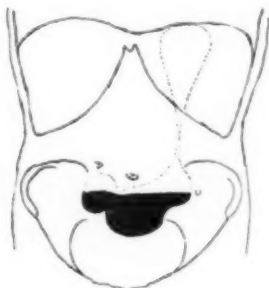


FIG. 2.

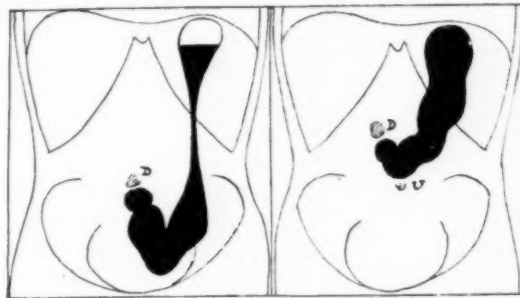
Pyloric obstruction due to duodenal ulcer; dilatation and hypertrophy of stomach. P, pylorus; U, upper level of gastric contents.

## (II) SITUATION OF THE STOMA ABOVE THE UPPER LEVEL OF THE GASTRIC CONTENTS.

In cases of extreme dilatation of the stomach I have, on a number of occasions, observed that in the vertical position the whole of the gastric contents accumulate in the lowest part of the stomach in such a way that their upper limit is below the pylorus, and may not even reach the lesser curvature (fig. 2). In such cases nothing at all can leave the pylorus, however strong peristalsis is, until the patient lies down. It is clear that in such cases an effective gastro-enterostomy must have the stoma so situated that it remains in the most dependent part of the stomach even when the vertical position is assumed. When the stomach is extremely dilated it must be exceedingly difficult to judge at an operation which will be the most dependent part when the



vertical position is assumed, as, quite apart from any dilatation, the influence of posture on the position of the stomach may be remarkably great (fig. 3). Fortunately, the rest in bed and the strict diet after the operation are a great safeguard: whilst lying down the stomach drains quite satisfactorily through the stoma, and consequently regains a great deal of its tone. I have, however, seen one case of dilated stomach due



Vertical position.

Horizontal position.

FIG. 3.

Gastroptosis. D, duodenum; U, umbilicus.

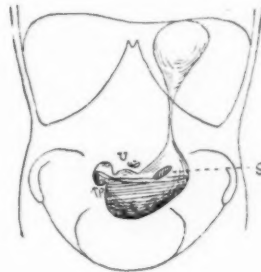


FIG. 4.

Gastro-enterostomy for pyloric obstruction: Stoma above the upper limit of the gastric contents in the vertical position. U, umbilicus; P, peristaltic waves; S, stoma.

to simple pyloric obstruction, in which no improvement resulted from operation, and in which we found that in the vertical position the upper limit of the gastric contents did not reach as high as the stoma or the pylorus (fig. 4), but that on compressing the lower part of the abdomen the contents rose above the stoma and at once began to pass

out of it (fig. 5). By supplying the patient with an abdominal support and making him lie down for an hour after meals on his left side—the position in which I found that the drainage was most rapid—complete relief was eventually obtained. A somewhat similar case has been described by Jonas.

I believe that the notorious absence of success of gastro-enterostomy, when performed for severe atonic dilatation of the stomach without organic obstruction, must be due to a similar cause, drainage through the stoma being mechanically impossible.

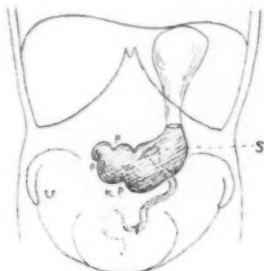


FIG. 5.

Same case as fig. 4, with abdomen compressed so that the gastric contents can pass out of the stoma.

#### REFERENCES.

- [1] HERTZ, A. F. "Constipation and Allied Intestinal Disorders," Lond., 1909, p.19.
- [2] JONAS, S. *Arch. f. Verdauungskrankh.*, Berl., 1908, xiv, p. 656.

#### DISCUSSION.

The PRESIDENT (Mr. G. H. Makins, C.B.) said all surgeons were acquainted with such after-histories after gastro-enterostomy. Perhaps Dr. Hertz's first class was, as the author himself said, most manageable. In reference to the second class, his impression was that if there was pyloric obstruction the patients eventually got well by treatment such as that which Dr. Hertz suggested. He remembered doing gastro-enterostomy years ago for a lady with long-standing symptoms of pyloric obstruction who had not eaten a solid meal for fifteen years. She seemed to be doing well after the operation, but after three weeks she recommenced to vomit up large quantities. It was clear that her stomach was not much improved by the operation. It was found that when the patient was placed on her right side the stomach emptied very

much better, and a truss was made for her which held the stomach up. She got well in a year, and he had since received a postcard from her every Christmas. He had not seen patients receive any benefit from the operation when it was performed for mere dilatation of the stomach. It was not easy to support the stomach in such cases and get the same result. He never did the operation for simple dilated stomach if he could avoid it; for though it did no material harm, it did not benefit the patients.

Mr. V. WARREN LOW said he thought surgeons should feel much indebted to Dr. Hertz for bringing the record of these cases forward, as well as for the explanation he had furnished. Many were perhaps familiar with the condition without having any explanation for it. He had long realized that patients who had had gastro-enterostomy performed and who were apparently satisfied with the result, had suffered somewhat from diarrhœa. In some cases they had not minded it much, because they had previously been constipated, and the inconvenience of the diarrhœa was comparatively small. He had heard of there being a sense of fullness after a meal, but he did not realize that it was due to distension of the jejunum; he thought it was some little recurrence of the condition for which the operation had been performed. He agreed it was deplorable to do the operation for a stomach which was merely flabby, without there being definite obstruction. He went further, for he would feel diffident about performing gastro-enterostomy for cases in which there was a duodenal kink. He had been persuaded to operate in such cases, but sometimes the patients had been subjected to a serious operation without the proportion of benefit which they had a right to expect. He had watched the case of one girl upon whom he operated for an enormous amount of gastroptosis. She had atonic dilatation of the stomach, and when a bismuth cachet was given her and the effect watched by X-rays, the cachet dropped from the œsophagus into a space in the region of the pelvis so suddenly that one's instinct was to look for it on the floor. The duodenum was more or less in its normal position, and he felt that the operation was justifiable owing to what seemed to be a fairly sharp kink at the pyloric end of the stomach, which might have acted as an obstruction. The patient was a lady's maid, and before the operation she at times had to leave whatever she was doing to retire to vomit copiously. Three months from her recovery she recommenced this vomiting, and X-ray examination showed that the stomach had not altered very much in position; the contents remained in very much the same place as before. Ultimately she was very much better; he did not know whether it was *post hoc* or *propter hoc*, but the improvement followed an operation for fixing a movable right kidney.

Sir FREDERIC EVE said his own experience in regard to the complications described was practically *nil*. He had only seen one case in which there was some diarrhœa after the operation, and she was a neurasthenic person. He agreed that after gastro-enterostomy the stomach was nearly always found to be hypertonic. He had watched afterwards practically all his cases of pyloric

obstruction, and all of them had done well. He agreed with Mr. Warren Low in regard to gastro-enterostomy in cases of gastroptosis; it should, in his opinion, never be performed. In many of these cases there was considerable kinking in the duodenum, but it could be got rid of by stitching the lesser curvature of the stomach to the gastro-hepatic omentum and diaphragm; and in gastroptosis occurring in young women brilliant and permanent results were obtained by this means.

Dr. A. E. RUSSELL said it would be interesting to hear how frequent was this recurrence of symptoms following the operation of gastro-enterostomy in the medical out-patient department; he did not see more than two or three cases a year of patients who came complaining of a return of symptoms. But perhaps such patients would be more likely to return to the surgeon who had operated upon them. When the operation had been done on account of definite pyloric scarring and dilatation of the stomach, the results seemed to him to have been particularly good. Any information such as he referred to would be useful as regards prognosis, especially as to the amount of improvement that could be promised when recommending operation.

Mr. SIDNEY BOYD remarked on the value of the paper and said that this would have been even enhanced if Dr. Hertz had stated what was the technique employed in the cases described. From the diagrams one judged that the opening was either transverse or oblique. He believed a vertical opening, with the lower end coming down to the greater curvature, gave the best results. In thirty gastro-enterostomies where he had done that he had not any of the after-results to which Dr. Hertz had alluded.

The PRESIDENT said he was familiar with the case of patients who came after gastro-enterostomy for so-called duodenal ulcer with symptoms very similar to those complained of before the operation. It was not correct to say that gastro-enterostomy was so much more successful for duodenal ulcer than for gastric ulcer. In the early days it was said that gastro-enterostomy would cure gastric ulcer; but that was a fable; nothing would cure an old chronic ulcer except removal. It must be remembered that patients with duodenal disease had long periods of immunity from symptoms, and then they would get dyspepsia or hæmorrhage again. But the interval of freedom might be as much as four or five years. He knew a patient who had had only two attacks of hæmorrhage in ten years. He was now fairly old, and when seen in the last attack was advised that when better he ought to be operated on. But the patient refused, and had not been troubled by the condition since. The interrupted character of the symptoms was probably a reason why gastro-enterostomy was said to be so efficacious for duodenal ulcer. He had no explanation for the cases he had seen with the symptoms mentioned by Dr. Hertz, and he did not even yet feel satisfied that the explanation given was the true one.

Dr. HERTZ, in reply, said he agreed that gastro-enterostomy for pyloric obstruction was an extraordinarily successful operation, so much so that he did not hesitate to recommend it in all cases at as early a stage as possible. He had only seen one instance of the second condition he described, but it was none the less important to recognize it, because it was so easy to convert an apparently unsuccessful case into a successful one by simply adopting the treatment he had detailed. The other condition he regarded as not uncommon, as he had seen about fifteen cases, in comparison with about five others, in which he thought there was recurrence of ulceration. He considered that the reason it was not still more often seen was that patients who had had such severe symptoms—pain after every meal, vomiting, and perhaps hæmorrhage—did not worry about symptoms which were often quite trivial in comparison. Yet if all patients were carefully questioned, as had been done in the collected statistics at several hospitals, the percentage of cases with complete freedom from symptoms would be found lower than had generally been thought. His impression was that, on the whole, a good result was more common in cases of duodenal than gastric ulcer, because in those cases the stomach was always hypertonic, whereas in gastric ulcer it was either of normal size or slightly enlarged. In duodenal cases, therefore, the stoma could work more efficiently. He agreed that gastro-enterostomy was not advisable in cases of gastropotosis. He believed the procedure of fastening the stomach up was also not often necessary. He had seen three cases—done by different surgeons—and on examining the stomach some time afterwards he found it was back in its old position, or only a trifle higher. In one instance he examined the patient just as she was leaving the hospital, feeling quite well; one expected to find the stomach high up under the liver, but it was exactly where it had been before the operation. The improvement in the symptoms was due to the fact that the patient had had four weeks' rest in hospital. The correct treatment for gastropotosis was rest; if these patients lay down after meals they were comfortable; if they remained erect they were not. With regard to atony of the stomach, gastro-enterostomy was also contra-indicated; if a patient had sufficient rest he would probably get well eventually. He thought that the only reason why the results of medical treatment were not more successful in these cases was that it was difficult to get the patient to take the needed two or three months' rest to restore the tone of the stomach.

Inferences on Modern Treatment drawn from Histories of  
Patients who have Recovered from the Perforation  
of a Gastric or Duodenal Pyloric Ulcer.

By EDRED M. CORNER, M.S.

IN the Erasmus Wilson Lectures, delivered before the Royal College of Surgeons of England, London, in 1903,<sup>1</sup> the pathological and clinical uniformity of gastric, duodenal, and other perforations of the alimentary tract was urged; the pathological process being termed an acute infective necrosis. In the *Journal of the American Medical Association* for August, 1908,<sup>2</sup> Dr. W. J. Mayo insists yet again on their clinical "oneness." The uniform character of the treatment also asserts the similarity of their characters. In the present communication I would suggest that it is most convenient to classify the ulcers particularly under discussion as *gastric* ulcers which are present at the cardiac end or in the body of the stomach, and *pyloric* ulcers, which term includes ulcers on either side of the pylorus—i.e., in the stomach or duodenum.

This classification suggests the partial giving up or limitation of the time-honoured words "duodenal ulcer," but is more practical than any other, gets over the difficulty of deciding if a particular ulcer is duodenal or gastric, and would serve, if others agree with me, to determine when the suture of a perforated ulcer is likely or not to require a gastro-enterostomy. The name "duodenal" would be retained for ulcers beyond the first part of the duodenum—i.e., the pyloric area.

There is already collected a vast literature on the subject of gastric and duodenal ulcers and their perforations, too large to be assimilable. But a great deal of this literature only serves to show that it is possible for a patient to recover from the perforation of a gastric or duodenal ulcer, and that the mortality of such an event varies, in general, directly with the time allowed to elapse between the perforation and the operation. Up to recently the main part of the operation performed consisted of suture of the ulcer. Operative procedures used by surgeons to combat such a perforation have been

<sup>1</sup> "Clinical and Pathological Observations on Acute Abdominal Diseases," 1904.

<sup>2</sup> *Journ. Amer. Med. Assoc.*, 1908, li, p. 556.

added to by the suggestion of Sir Berkeley Moynihan, of Leeds,<sup>1</sup> that a gastro-enterostomy should be performed at the same operation as that at which the ulcer was sutured. This addition to the operation on a patient often already perilously ill cannot be accepted without very strict examination. Indeed, the opponents to its introduction referred to it as an exhibition of surgical agility at the expense of the patient.

It is a matter of common clinical observation which must come before the notice of every surgeon that some patients in whom the perforation of a gastric or duodenal ulcer has been successfully sutured do very well, lead busy, useful lives, and with exception, perhaps, of occasional dyspepsia, are quite well. It might well be asked, how could a gastro-enterostomy possibly benefit such people? Yet Sir Berkeley Moynihan is not a man to "say it very deliberately" (his own words)<sup>2</sup> and advise the performance of a gastro-enterostomy without good reason. This was advised in the discussion on operations for gastric ulcer before our predecessors, the Medico-Chirurgical Society, in 1907. Five years have now elapsed, and during that time sufficient evidence must have accumulated to shed light on this point and enable us to see in what degrees both Sir Berkeley Moynihan and his opponents were right. I have therefore surveyed the literature on this subject since 1907, and have followed up (even to the employment of a private detective) as many patients as I could who have recovered from an operation for the perforation of a gastric ulcer. For permission to use their cases I must thank my colleagues, past and present, at St. Thomas's Hospital. These cases, forty in number, were in the Hospital between 1900 and 1910.

Of them, about one-third (33 per cent.) were completely cured. The remaining two-thirds (67 per cent.) were unsatisfactory on account of dyspeptic attacks, inability to follow their occupations, the necessity of constant care in their diet, nervousness, depression, and so forth. I have given so rough an estimate of the condition of these people after operation because if another person were to make another and similar estimate from the same lot of patients he would form a different opinion. The reason for this is that he would regard, and perhaps quite rightly, many of my "unsatisfactory two-thirds" as satisfactory. This is well shown by the estimates of other authors.

<sup>1</sup> *Med.-Chir. Trans.*, 1907, xc, pp. 254-57.

<sup>2</sup> *Ibid.*, p. 254.



## OTHER AUTHORS.

|   |   |                          | Satisfactory | Unsatisfactory |
|---|---|--------------------------|--------------|----------------|
|   |   |                          | Per cent.    | Per cent.      |
| 1 | <i>Guy's Hospital Reports</i> , 1907, lxi                   | French (18 cases)        | 83           | 17             |
| 2 | <i>Medico-Chirurgical Transactions</i> , 1903               | Crisp English (17 cases) | 65           | 35             |
| 3 | <i>Lancet</i> , 1906  | Paterson (33 cases)      | 48           | 52             |
| 4 | <i>British Medical Journal</i> , 1910                       | Morton (11 cases)        | 30           | 70             |
| 5 | <i>Bristol Medico-Chirurgical Journal</i> , September, 1911 | Rendle Short (23 cases)  | 34           | 66             |
| 6 | <i>Proceedings of the Royal Society of Medicine</i> , 1913  | Corner (40 cases)        | 33           | 67             |

One hundred and forty-two cases in all.

The great variation in these estimates, from Dr. French in 1907 (83 per cent.) to that of Mr. Morton, of Glasgow, in 1910 (30 per cent.), is due to the widely different views which can be taken quite intelligently of what is to be regarded as satisfactory and what is decided to be unsatisfactory. I have therefore formed a modest estimate, by chance following Mr. Short and Mr. Morton, of complete and incomplete cures. In this estimate the three of us (Short, Morton, and Corner) agree very well, and our results, based on seventy-four cases altogether, only show divergence from the other observers in degree, not in the principle involved. Hence it can be assumed that as one-third of the successful cases of the perforations of a pyloric ulcer are cured, a gastro-enterostomy done at the same operation as that in which the ulcer is sutured could have done the patients no good, and have been entirely an exhibition of "surgical agility at the patients' expense." Indeed, it would and must have done some of the patients harm, as we must all know of patients who have been made chronic invalids by the operation of gastro-enterostomy. Hence it is obvious that no gastro-enterostomy is required in at least one-third of the cases of the perforation of a gastric or duodenal ulcer which come to operation. To try and find out why some patients are cured and some are not, I have gone carefully into the notes of the St. Thomas's Hospital and private patients; as a result of this study I would suggest that the patients owe their cure largely to two factors:—

- (1) The situation of the ulcer.
- (2) The pathological character of the ulcer.

(1) *The Situation of the Gastric Ulcer*.—Those patients who became completely cured after the operation, as contrasted with those who did

not, show a far greater proportion of ulcers situated in the cardiac end of the stomach. Whilst the patients whose perforated ulcers were pyloric and duodenal showed greater likelihood of their becoming the subjects of pain and dyspepsia or recurrent ulceration after operation, nothing can be said so definitely as to the influence of the situation of an ulcer on the anterior or posterior wall of the stomach, or on the greater or lesser curvature of the stomach. But it does seem reasonably certain that ulcers in the cardiac and body of the stomach offer a far better chance of complete cure than do ulcers in the neighbourhood of the pylorus, whether they be on the anterior or posterior wall or on either curvature. The former do not, therefore, require a gastro-enterostomy, which will find its sphere of usefulness amongst pyloric ulcers. Mr. T. Crisp English,<sup>1</sup> in his paper in 1903, says that these perforated ulcers existed to each other in the proportion of 54 per cent. of cardiac ulcers to 46 per cent. of pyloric ulcers, which suggests that a gastro-enterostomy may be required in about one-half (50 per cent.) of the cases operated on for perforated gastric ulcer. Mr. Alexander Miles,<sup>2</sup> of Edinburgh, has, not unnaturally, differed in his estimate from that of Mr. Crisp English, making 50 per cent. of perforating ulcers cardiac and 50 per cent. pyloric. Amongst perforated pyloric ulcers (gastric and duodenal), some patients recover completely. Hence one is quite safe to say that a gastro-enterostomy is not required in as many as half the cases of the perforation of a gastric or duodenal ulcer.

(2) *The Pathological Character of the Ulcer.*—That gastric and duodenal ulcers vary in their pathological character everyone knows and no one will deny. Now there is a variety in which the tissue death, which constitutes the perforation of the ulcer, is the last phase of the disease, leaving the walls of the ulcer ready to heal. Hence, when it is sutured it heals firmly, never breaks down again, or by infection gives rise to satellite or recurrent ulcers. In consequence the patient gets completely well after the operation for the suture of the perforated ulcer. Apparently these ulcers occur in both ends of the stomach and in the duodenum. From our lack of knowledge at present we cannot differentiate them from the more troublesome ulcers, but we suspect them of being present as an acute ulcer in a patient who has had little or no symptoms before the perforation. In such cases a gastro-enterostomy is not required.

<sup>1</sup> *Med.-Chir. Trans.*, 1904, lxxxvii, pp. 27-51

<sup>2</sup> *Edin. Med. Journ.*, 1906, N.S., xx, pp. 106, 223.

Hitherto this paper has been concerned with negative propositions so far as the operation of gastro-enterostomy is concerned, and it is only right that some attempt should be made to show what evidence St. Thomas's Hospital can produce as the result of the five years which have elapsed since the great discussion on the treatment of gastric ulcers before the Royal Medico-Chirurgical Society in 1907.<sup>1</sup> In the first place, it has been proved that to do an operation of gastro-enterostomy at the same time as the coeliotomy for suturing the ulcer may be more than the patient can withstand. One death at least may be attributed to this excess of zeal. On the other hand, it is clear that a great many patients who had an immediate gastro-enterostomy became completely cured. Was it due to the gastro-enterostomy? Then there are some who are not completely cured in spite of the gastro-enterostomy. Is this due to the gastro-enterostomy? Further, it is very far from proved that the recovery-rate for the operation of suture of the ulcer and primary gastro-enterostomy was higher or lower than that consequent upon coeliotomy and suture. And it is not clear in any way that a primary gastro-enterostomy is better than a secondary gastro-enterostomy (three to six months or more later), indeed a secondary gastro-enterostomy apparently has made some unsatisfactory cases eminently satisfactory, but not always. Even this benefit cannot be attributed with certainty to the gastro-enterostomy, because some women who had recovered from the perforation of a gastric ulcer and were unsatisfactory on account of dyspepsia, constipation, flatulence, &c., became eminently satisfactory after marriage and its consequences; a change of living curing them.

Thus, to sum up the results of my examination of some forty cases and five years of literature, it would seem that:—

(1) Many subjects of the perforation of a gastric ulcer are benefited by a gastro-enterostomy. This is particularly true if the perforating ulcer is in the neighbourhood of the pylorus, gastric or duodenal.

(2) It would appear, speaking generally, that a secondary gastro-enterostomy—i.e., after the patient has recovered from the immediate danger of the perforation—is better than a primary gastro-enterostomy.

(3) It is better for the patient to have a secondary gastro-enterostomy when it is required than have the additional danger of a primary gastro-enterostomy which may not be needed. It would appear that the "betting" is rather in favour that it—the gastro-enterostomy—would not than that it would be needed.

<sup>1</sup> *Med. Chir. Trans.*, 1907, xc, pp. 217-414.

(4) It has not been shown that a primary gastro-enterostomy presents such advantages over a secondary gastro-enterostomy that it—the primary gastro-enterostomy—should be practised in the treatment of the perforation of ulcers even when situated in the neighbourhood of the pylorus.

#### POST-OPERATIVE DYSPEPSIA.

In the course of my study of these cases I have naturally met with features of interest which I will briefly narrate. There is a clinical point of great moment in the history of patients who have recovered from the perforation of a gastric ulcer. It is very common for these patients to have an attack, often a long one, of pain and dyspepsia, beginning a few months after the operation. For instance, there is the case reported by Mr. Parsons,<sup>1</sup> of Dublin, of a girl, aged 19, who recovered from the perforation of a gastric ulcer and had an attack of "pain and dyspepsia" six months after the operation, and from which she was not free for about eighteen months. She never required a secondary gastro-enterostomy, and when once the pain had disappeared it went for good, leaving her in an eminently satisfactory condition about two years after the operation. Personally, I have seen three patients whose "post-operative" dyspepsia was so bad and prolonged that I advised a secondary gastro-enterostomy; yet with medical means they were cured, and have remained cured, none requiring operation. Death from the perforation of a second ulcer generally is limited to a single instance in each published series of cases, as Dr. French<sup>2</sup> has pointed out. There was one such instance amongst the author's series of cases. Hence it may be regarded as known, but uncommon. Indeed, it seems less common than the perforation of a jejunal ulcer after a gastro-enterostomy, and I think it is clear that this phase of "post-operative" dyspepsia is eminently capable of cure by medical means. In fact, I would urge that it is anticipated by medical treatment and advice in every case of recovery from the perforation of an ulcer. In my experience it is far more common than is the need for a secondary gastro-enterostomy.

Before closing this section of my communication I would like to say that, certainly with regard to the cases concerned in this paper, appendix dyspepsia is of no great moment, but often it is well to remove the appendix when doing a secondary gastro-enterostomy.

<sup>1</sup> *Dublin Med. Journ.*, 1906, cxxi, pp. 81-92.

<sup>2</sup> *Loc. cit.*

## OCCLUSION OF THE PYLORUS.

In connexion with gastro-enterostomies, primary or secondary, done for the relief of ulcers in the neighbourhood of the pylorus, there is a very important point in technique which I would submit for your consideration.

All fluid of which the habit is to pass along a pipe has comparatively little tendency to escape through a lateral hole in that pipe; or, to put it another way, even when a lateral aperture is present, the great volume of the fluid will continue to flow along the pipe, and but comparatively little will escape through the lateral opening. A gastro-enterostomy is merely a lateral opening, and in consequence through it only a small proportion of the gastric contents will pass, especially of the lighter and fluid contents. Hence, without pyloric obstruction, a gastro-enterostomy is no panacea for ulcers in the neighbourhood of the pylorus or duodenum. This was excellently illustrated by a patient under the care of Dr. Mason, of Boston, Lincolnshire. The patient had a gastro-enterostomy done by Sir Berkeley Moynihan—a guarantee that it was well done. During the next four years the patient had pains, dyspepsia, and discomfort. At the end of that time, in Sir Berkeley's absence, I had to open the abdomen hurriedly. There was no jejunal ulcer present; indeed, the gastro-enterostomy opening was very contracted. But the patient had a large perforated ulcer in the first part of his duodenum. This case illustrates that the ulcer probably was not cured by the gastro-enterostomy; again, that in the absence of pyloric obstruction a gastro-enterostomy tends to close (like any other lateral anastomosis not in the presence of obstruction to the flow directly onward). Then I may mention another instance: A young woman was successfully operated upon by Mr. H. Sampson for me at the Bowes Park Cottage Hospital for the perforation of a pyloric ulcer. No gastro-enterostomy was done. A year later Mr. L. E. Barrington Ward operated again, and again successfully, for the perforation of a pyloric ulcer. A secondary gastro-enterostomy was done later, and so far it works well. I would suggest that this is largely due to the presence of adhesions in the neighbourhood of the pylorus causing obstruction. A better illustration is that of a young man who was successfully operated upon for a gastric ulcer, a primary gastro-enterostomy being done. After a year of pain and discomfort it was needful to explore the abdomen again. The gastro-enterostomy was found to be excellent, and there was no trace of a jejunal ulcer. Hence, the cause of the patient's pain and discomfort

was most probably the passage of the gastric contents over the region of the former ulcer which had perforated—i.e., in the neighbourhood of the pylorus. These gastric contents could be made to pass through the gastro-enterostomy opening by occluding the pylorus. Therefore, a ligature of silk was passed round the pyloric end of the stomach and tied sufficiently tight to occlude the lumen. The effect of this simple proceeding on the man's pain was simply magical. When he came round from the anaesthetic the pain was gone! This occlusion of the pylorus was first suggested by Berg. Since this date I have always placed a ligature on the pyloric end of the stomach when

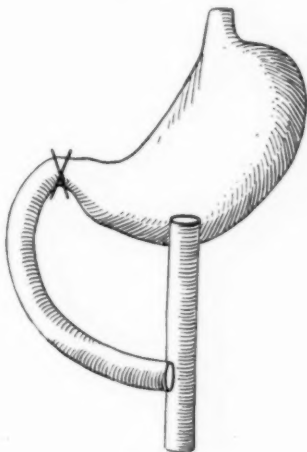


FIG. 1.

Occlusion of the pylorus by a silk ligature, combined with a Roux's gastro-enterostomy.

doing a gastro-enterostomy for pyloric ulcers (or when the ulcers were believed to be pyloric), and I think that the patients have benefited therefrom. Further, I would like to say that, when the patient's condition allows of it, I have had better results from a posterior gastro-enterostomy done after Roux's method than any other. The phrase "after Roux's method" has been used, as I believe that an anterior gastro-enterostomy was an essential part of Roux's original plan, whilst I have always used a posterior gastro-enterostomy. After it there is no vicious circle or regurgitation of bile into the stomach, and the operation is not marred by the "no loop" fallacy. In default of

being able to do a Roux's gastro-enterostomy I believe that it is better to do an entero-enterostomy and place a ligature, not tightly, on the afferent loop of the jejunum between the entero-enterostomy and the stomach, as first suggested by Fowler. This can be done at the first operation, primarily, the patient's condition permitting; or later, secondarily. But, usually, it is better done than left undone. Occlusion of the pylorus may be followed by much vomiting during the first day or two after operation if food is given, and, owing to temporary swelling, the gastro-enterostomy aperture is closed. In such cases the patient is given continuous infusion of saline *per rectum* and no food by mouth. Later water is given in small doses.

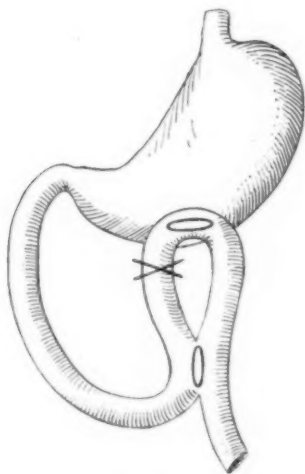


FIG. 2.

Occlusion of the afferent loop combined with an entero-enterostomy by the ordinary method.

Recently, I have under my care an elderly gentleman, aged 63, who has been operated on already twice, for appendicectomy and for an ileo-cæcal kink with intestinal stasis. The poor fellow really has a large duodenal ulcer adherent to his liver and pancreas (? carcinoma). For this I did a gastro-enterostomy with occlusion of his pylorus, with considerable amelioration of his condition.

From the brief notes I have given I would submit that occlusion of the pylorus is a very real measure to be considered as a valuable, or even a necessary, adjunct to gastro-enterostomy performed for the relief of pyloric (and duodenal) ulcers. As such I bring it to your notice,



## ISOLATION OF THE PERFORATION BY TAMPONADE.

Undoubtedly the best local treatment for a perforated gastric or duodenal ulcer is to close it by suture and the abdomen without drainage. But there can be no doubt that one of the first difficulties which a surgeon meets in these cases is to close the perforated ulcer soundly and satisfactorily. The reason of the difficulty is that the stitches used to close the perforation "cut through" the sodden, swollen tissues in which they have to be inserted to close the perforation. If such "cutting through" happens under our very eyes, how often does it result in the loosening or the total loss of hold of the stitches on the tissues after the abdomen is closed and the patient is in bed? One cannot but surmise that many perforations deemed to be closed satisfactorily at the operation are not so an hour or two later. Yet in spite of this, patients who have been operated upon continue to recover. Hence there is a justifiable suspicion that cases of perforated gastric or duodenal ulcer can recover when the perforation is not closed; or, at least, imperfectly closed. In 1908, Mr. Walter R. Bristow and I<sup>1</sup> put this to the test in not attempting to close the perforated ulcer in two patients: in one we "corked" the perforation with a tag of omentum, and in the other a veil of omentum was maintained in position by two or three stitches. Both patients recovered and had easy convalescences, unmarked by any feature, such as gastric fistula, which would suggest leaking through the perforation. Since this date (1908) I have used the principle of isolating but not closing the ulcer on at least fifteen occasions, including one perforation on the posterior gastric wall. In two of these the end of a gauze plug was held by a catgut stitch in the aperture of the perforation. I have never lost a patient on whom this practice has been used. These patients have done uniformly well. Personally, I think better than do those on whom time was spent in closing (?) the ulcer by suture. As a general rule, the longer the time spent in suturing the perforation the greater the difficulty and the insecurity of the closure. Isolation of the perforation by tamponade has the advantage of being simple and of saving valuable time. No patient on whom it was done has ever needed a primary or a secondary gastro-enterostomy. No patient has had a gastric fistula, or has in any way, such as by delayed convalescence, shown sign (or signs) of the non-closure of the ulcer. I may add that when the perforation is not sutured the end of a gauze drain is always placed next the ulcer and

<sup>1</sup> *Brit. Med. Journ.*, 1909, i, p. 1288.

brought out of the wound. This drain is removed in about thirty-six hours under anæsthesia with nitrous oxide gas, and not replaced. After operation the patient is placed in the Fowler position, saline solution is administered rectally and continuously, and nothing but water is given by mouth for two or three days. Recently it has been my practice to enclose the isolating tampon of gauze in a longitudinally split rubber tube, a cigarette drain, part of which is left in position after the removal of the gauze.

Having shown the practicability of the successful isolation of a perforation with a gauze tampon, it may now be discussed what possible position may be taken by this procedure in the surgery of perforated gastric and duodenal ulcers. I would suggest this: The firm closure of the perforation and of the abdomen is undoubtedly the best treatment that can possibly be carried out. But this ideal is in practice more often unrealizable than realizable. Therefore, I would suggest that at first an attempt be made to close the perforation by suture. If this fails, or appears to afford a doubtful closure of the perforation, no further time should be spent on it, but the ulcer plugged and drained. This I would suggest, having first proved that it can be done successfully; tamponing the perforation with omentum and gauze is the second best line of treatment for the perforation of a gastric or duodenal ulcer; and this second line of treatment is of much more frequent and general application than is the first. Indeed, the patients I have deliberately tried it upon have done so well that I believe, chiefly on account of its saving time, the isolation of these ulcers by tampon will become the first and most popular line of treatment except in cases operated upon very early after perforation of the ulcer.

#### SUBACUTE PERITONITIS, CHRONIC PERITONITIS, AND ADHESIONS.

All are familiar with complications such as pelvic abscess or sub-diaphragmatic abscess, but we are not so familiar with the course of a subacute or chronic peritonitis which may go on for weeks, and against which vaccine and serum treatment is the sheet-anchor of our treatment. Let me quote an example: I operated for the perforation of a gastric ulcer in a girl, aged 21, about forty hours after the perforation. The perforation was closed by suture and its track isolated from the rest of the peritoneal cavity by omentum and a gauze drain. The pelvis and loins were dried through a sub-umbilical incision and the former drained. For between five and six weeks that patient kept having

a very regular temperature, about 100° F. No signs of a residual abscess in the loins, pelvis, or sub-diaphragmatic spaces were discoverable. There was nothing in the pleura or pericardium. Some albumin appeared in the urine. The bowels acted well and food was taken. The abdomen was somewhat distended. There was a large leucocytosis. The left sub-diaphragmatic region was explored in the hope of discovering an abscess, but only a large spleen, surrounded by perisplenitis, was found. Suffice it to say that the patient succumbed in spite of all treatment after an illness which lasted six weeks.

Then I have the case of a man who had a perforated gastric ulcer which was operated on some twelve hours after the perforation. Owing to the œdema of the tissues round the perforation it could not be closed satisfactorily. This man has had a subacute or chronic peritonitis going on for twelve weeks, and from which he recovered slowly. The chart shows well the duration of the case and the irregular character of the fever.

Consideration of these last two cases leads me to that of my first successful operation for the perforation of a duodenal ulcer (1901). The case illustrates a result of the peritonitis which may follow the perforation and be recovered from. An infinity of adhesions causing death is sufficiently unusual in these cases as to be worthy of record, the adhesions in general clearing up marvellously.

In July, 1901, a physically perfectly developed man, aged 34, was admitted to St. Thomas's Hospital. He never had anything the matter with him until he had abdominal pain four days previously. This pain increased, and there was no onset of symptoms which would suggest the sudden perforation of an ulcer. At the operation a perforation  $\frac{1}{3}$  in. in diameter was found about  $\frac{1}{2}$  in. on the duodenal side of the pylorus. This was closed by sutures and the peritoneum washed with saline solution. After operation the temperature was irregular for seven days, reaching to between 100° and 101° F.; on the sixth day it reached 101·4° F. The stitches were removed on the tenth day and the wounds were clean. He had slight diarrhoea. Beyond this his convalescence was without incident. In December, 1901, he was readmitted to the hospital for abdominal pain and obstinate constipation, which rendered him miserable, and has caused him to seek refuge in alcohol. At operation it was found that every item of the alimentary canal was superlatively adherent to its surroundings, but not to the abdominal wall or the scars. In other words, his symptoms were due to superlative visceral adhesions. There were no signs of tuberculosis now or at his first operation. The man died about a fortnight after the exploratory operation.

Such a condition must have been the result of a widespread form of peritonitis arising in some "lowly" form of infection from which at first the man recovered, but was unable to regain sufficient power to "clear up" the adhesions, which led to his death in six months' time. The case has been brought forward from other points of view in the Erasmus Wilson Lectures of 1903.<sup>1</sup>

#### VENTRAL HERNIE.

Examination of the patients who had recovered from an operation or operations for the perforation of a gastric or duodenal ulcer showed two facts about ventral hernia which are well worth consideration. Firstly, it may be premised that ventral herniæ are not infrequent after an operation for the suture of a perforated gastric or duodenal ulcer. Secondly, where two incisions were present, it was more frequent to have a hernia through the scar in the upper abdomen than through that in the lower abdomen. This fact is a reversal of the generally accepted dictum that ventral herniæ are more prone to follow scars in the lower than in the upper abdomen. Thirdly, the hernial protrusions through the scar in the upper abdomen were larger in general than those in the lower abdomen; but though more frequent and larger they do not give rise to so great a sense of weakness, disability, or discomfort as the latter do. From this follows another clinical feature—namely, when a patient complains of symptoms referred to the hernial protrusion, in all probability they are due to conditions (of the stomach) underneath. Thus in one patient who came complaining of symptoms which he referred to the hernia, Dr. H. P. Hawkins found the signs of a dilated stomach and pyloric obstruction. A gastro-enterostomy relieved the symptoms of which he complained, but the hernial aperture was too large to be closed by suture, and so the hernia persisted, definitely and tritely proving that the symptoms were not due to the hernia, but to the pyloric obstruction beneath.

In conclusion, I would like to lay emphasis on what is a fairly obvious fact. Patients who have undergone such nervous shock as that accompanying the perforation of and the operative procedures for the perforation of a gastric or duodenal ulcer are extremely prone to become neurasthenic; so that they could not do what they used to do formerly, having to give up their occupation (such as of a painter, &c.). There can be no doubt that this neurasthenia, and the brevity of convalescences

<sup>1</sup> "Clinical and Pathological Observations on Acute Abdominal Diseases."

in modern surgery, which is inseparable from the condition under discussion, has a great deal to do with the occurrence of dyspepsia and pain after the illness, such as that shown by those patients who were relieved by a marriage. This consideration makes the very various opinions of those who have worked at the condition of patients after recovery from the perforation of a gastric or duodenal ulcer comprehensible, and it must make us very careful not to recommend a secondary gastro-enterostomy for neurasthenia. So far as I have been able to discover, patients who have had a primary gastro-enterostomy are just as neurasthenic as those who have not.

#### DISCUSSION.

Dr. HERTZ said he was pleased to hear the conclusion to the first part of the paper—namely, that it was best not to do gastro-enterostomy as a primary operation in those cases. He had always thought it was wasting valuable time to do more than was absolutely necessary. The return of symptoms could be to a great extent prevented if people were to realize that there was such a thing as an "ulcer diathesis"; a patient who had once had ulcer being more liable than the average individual to gastric and duodenal ulceration. It was easy to cure a patient of an attack of duodenal or gastric ulcer by rest in bed and suitable diet, but many of these patients had recurrences months or even years later. Recognition of this liability to recurrence would lead to such careful instructions being given as to mode of life and diet that the danger would be much lessened. One point in the paper about which he was doubtful was as to the theoretical arguments about the action of the stoma after gastro-enterostomy. It was said that a tube with an outlet at the side would nevertheless empty itself at the terminal outlet. Actually, he believed, that was not so. It was difficult to get people who had had gastro-enterostomy done with a satisfactory result to return for further examination; but he had managed to do so in about ten cases, and had examined them with the X-rays. In all these satisfactory cases the stoma was acting, though in none had the pylorus been obstructed; the greater part of the food was passing through the stoma and only a small amount through the pylorus. The ideal result of gastro-enterostomy appeared to be for two-thirds of the chyme to pass through the stoma and one-third through the pylorus. In the cases described in his paper that evening, everything passed through the stoma, and that too rapidly. In the successful cases after duodenal ulcer, though the pylorus was quite patent, two-thirds passed out of the stoma. Therefore it did not seem that there could be much advantage in putting a ligature round the pylorus. He asked whether there was any evidence as to the final result of ligaturing, because from experiments of tying a ligature round the gut of animals it was

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found that it cut through so that the lumen was restored. He did not think that tying a ligature round the pylorus could obliterate it and cause permanent obstruction.

Sir FREDERIC EVE said Mr. Corner had given valuable indications as to when gastro-enterostomy should be done in perforating ulcer of the stomach. Mr. Corner suggested that in cases of acute ulcer gastro-enterostomy was not required. The condition could mostly be ascertained by palpation, for in chronic ulcer there would be more marginal thickening. He had always held that a primary gastro-enterostomy was not necessarily a feature of the operation for perforating gastric ulcer; and it was not as a definite rule desirable to add something more to what was already a serious condition. Therefore he usually preferred to postpone gastro-enterostomy to a later period. He had been much interested in hearing what Dr. Hertz said about the passage of food through the pylorus after gastro-enterostomy with a patent pylorus. That did not agree with the original observations of Cannon, but coincided with the few cases in which he investigated the stomach with the X-rays. He had occasionally performed the operation of occlusion of the pylorus in cases of duodenal ulcer, but not as a routine measure; though theoretically it might be the right thing, he had arrived at the conclusion that it was not really necessary. When he had employed it, he had not passed a ligature round the pylorus, but a series of reef sutures at intervals round the pylorus; these, when tied, occluded the lumen. With regard to the cases in which one should use an omental graft and tamponage, he believed that one could easily tell by the condition of the stomach wall round the ulcer whether the sutures would hold. Suture and infolding was the ideal method; but if there was considerable and widespread thickening of the stomach wall he agreed with Mr. Corner it would be better to put in an omental graft, and use a drain or a tampon.

The PRESIDENT (Mr. G. H. Making, C.B.), said he felt doubtful about supporting the method of plugging, and it was risky to encourage others to use a plug. In the early days, when it was found difficult to suture, his experience had been that when closure was not effected the patients died in spite of drainage. Covering with omentum he took to be the same in effect as suturing. In a general way, most ulcers could be sutured; if the ulcer was an old one and this could not be done, it was often possible to remove it, and such had been his practice. He had several times excised the ulcer after perforation had occurred, and the patients had recovered without difficulty. The ideal method in any case was to close the stomach or the duodenum, when the opening could be discovered.

Mr. CORNER, in reply, said he could not answer Dr. Hertz's question exactly as to the final results of occlusion of the pylorus by ligature, as sufficient time had not yet elapsed to enable him to ascertain such results from his own patients. He hoped that the lightly tied silk would form a foundation for the formation of a more permanent ring of fibrous tissue.

## Surgical Section.

March 11, 1913.

Mr. G. H. MAKINS, C.B., President of the Section, in the Chair.

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### Ligature of the Renal Artery and Vein as a Substitute for Nephrectomy.

By THOMAS H. KELLOCK, M.C.

SOME year or two ago I read in one of the medical journals (the *Lancet* I believe) a short account of an operation that had been performed in India by a surgeon either in the Army or Indian Medical Service, consisting of the ligature of the renal artery and vein by the abdominal route as a substitute for nephrectomy. If I remember rightly, the pathological condition of the kidney in that case was due to tuberculous disease, and the condition of the patient such as to negative the more serious operation of nephrectomy. I have made and had made for me careful search to discover the account of that operation, but I am sorry to say without success, and so I must now offer my apologies to its author for my inability to give him by name the credit I should like to, for I believe his was the first case recorded where the operation was done deliberately with the object of starving a diseased kidney, although I believe it has been performed for renal aneurysm.<sup>1</sup> No one reading the account of that operation could fail to recognize what a very useful proceeding it might be found in suitable cases. It was not, however, until recently that I had the opportunity of putting it into practice, when the case, the notes of which I am about to read, presented itself, and seemed to be exactly one in which it might prove to be of great value.

<sup>1</sup> Since this paper was printed my attention has been called to the paper of Major M. P. Holt, R.A.M.C., in the *Med. Chir. Trans.*, 1907, xc, pp. 469-78, which is evidently the paper referred to above.—T. H. K.



The patient was a native of India, aged 30, a clerk by occupation; he had made the journey to England in the hope of being cured of a very distressing condition. He gave the following history: In the year 1910, whilst in India, he suffered from vesical calculus; this was removed by the perineal route with apparently complete success, except that at times he had not complete control of the passage of urine. Later in the same year he began to suffer pain in the left lumbar region, and after a month of rather severe suffering an operation was performed, and an abscess opened in this situation. Several incisions appear to have been made before the abscess was found, for he said that some of them healed up at once, but one remained open and discharging fluid, the nature of which he did not know. In November, 1910, another operation was performed; the wound was enlarged, but he did not know what further was done except that a part of the lowest rib was removed. This did not bring about closure of the wound, which had continued to discharge pus until he arrived in England.

He was admitted to the Middlesex Hospital under my care on August 31, 1911, in an extremely emaciated condition, complaining of pain in the left lumbar region and frequency of micturition; the urine was small in amount (averaging only 26 oz. *per diem* during the first six days he was in the Hospital) and was passed frequently in small quantities with some pain; it was acid and contained a good deal of pus. A healed scar in the perineum showed where lithotomy had been performed; in the left lumbar region there were several long scars: two of these, which crossed at right angles, were near the crest of the ilium, and one just over the situation of the twelfth rib; about midway between these was a sinus in the centre of a scar, somewhat sunken, surrounded by densely hard fibrous tissue and discharging a quantity of foul-smelling pus. There was only slight tenderness in this region, and as far as examination could be made the kidney did not appear to be much enlarged. A skiagram showed the presence, apparently in the kidney, of a calculus of some size, and also a shadow of what proved to be a short piece of india-rubber drainage-tube.

A few days after admission the patient was anæsthetized and an examination made of the sinus; a probe passed inwards in the direction of the kidney and was felt to grate against the calculus. A pair of forceps was then passed and with them the piece of drainage-tube was felt and removed. An attempt to grasp the calculus was followed by an alarming gush of arterial blood which flowed with considerable force. A free incision was rapidly made backwards and forwards from the sinus,

and the calculus, which was about the size of a pigeon's egg, removed with forceps, very considerable hæmorrhage taking place all the time this was being done. Immediately the stone was removed gauze swabs were tightly packed into the bottom of the cavity where this had lain, and fortunately the hæmorrhage was completely arrested. No further bleeding took place, although after the second day there was a good deal of offensive purulent discharge from the wound. The urine at this time contained a good deal of pus and blood, in quantity it remained much the same as before the operation.

Eighteen days later the abdomen was opened through the upper part of the left rectus muscle with the intention of ligaturing the renal artery and vein. After turning the patient on to his right side and displacing the small intestines to the right the parietal peritoneum was incised over the situation of the vessels and these sought for; finding them was a matter of difficulty, for all the tissues in the neighbourhood were hard and matted with inflammatory products which had spread from the kidney, and the original intention of ligaturing the vessels separately had to be abandoned. Pulsation could be felt in the situation of the renal artery, so an aneurysm needle was passed under this, going rather wide of it on either side, and a ligature passed and tied, which it was thought should include both artery and vein. An examination of the kidney was then made from the lumbar wound, when it was found that the finger could easily be passed into the pelvis of the kidney.

For a few days after the operation the urine contained pus and blood, and a good deal of offensive discharge, which smelt urinous, came from the lumbar wound. Ten days later the urine was free of pus or blood, and increased considerably in quantity.

The abdominal wound healed by first intention, but the lumbar sinus continued to discharge. Nine weeks later the sinus in the loin was still open but discharging very little. The patient had improved very much, and had put on a good deal of weight. The urine was quite normal.

An anæsthetic was administered and the sinus explored. On passing a finger down to the region of the kidney a mass of this was felt projecting and very easily broke off and came away, and in this way several more masses were broken off and removed. The pieces that came away were very friable, almost quite white, and on squeezing were found to contain no blood. A large part if not quite all of the kidney came away in this way.

After this last operation the sinus closed and the patient left the hospital about five weeks later. He was seen some months afterwards

when he was about to return to India. The sinus was firmly closed; he had increased very much in weight, and was in good general health.

Performed on the cadaver when the parts concerned are not diseased, ligature of the left renal artery and vein is not a very difficult matter. By making the incision through the abdominal wall a little to the left of the middle line, then turning the body on to the right side so that the small intestines fall away to the right, and opening the peritoneum posteriorly at a point about 3 in. above the level of the umbilicus, the artery can be felt lying against the side of the vertebral column with the vein in front of and a little below it, and they can easily be ligatured together or separately in this position. A point which struck me in two cases where I performed the operation on the cadaver was the rather large amount of cellular tissue between the peritoneum and the vessels which had to be torn away before the latter could be satisfactorily isolated. On the right side the operation is considerably more difficult on account of the presence of the second part of the duodenum and the head of the pancreas. I attempted it on one occasion for extensive tuberculous disease of the right kidney, but had to abandon it, as I found it impossible to get anywhere near the vessels on account of extension of the disease along them. The operation on the left side is, as I have said, easy when the parts are unaffected by disease, but this will rarely be the case when the operation is called for, and in the case I have narrated the products of old inflammation were so dense that it was impossible to recognize the vessels individually, and I had to resort to a ligature passed round both of them in the position where the pulsation of the artery could be felt. That the ligature served its purpose was evident from the result. Under such conditions this would seem to be the best course, for dissection to differentiate the vessels would prolong the operation, and would probably be rendered even more difficult by hæmorrhage from the dissected parts.

One has, of course, to bear in mind the possibility of the presence of abnormal or additional arteries supplying the kidney, which, if present, might defeat the object of the operation, and they would be difficult to detect during its performance. In the case I have related the operation fulfilled its purpose excellently; on the left side, at any rate, it is a much simpler proceeding than nephrectomy, and it has also the great advantage that it can be done as a clean operation, even though the kidney itself be septic. Its applicability must, of course, be limited, but in suitable cases it would seem to be very justifiable and useful.

## DISCUSSION.

Mr. CHARTERS SYMONDS congratulated Mr. Kellock upon his success in the operation he had mentioned in his paper, and thanked him for introducing to them a method of operation in difficult cases which was certainly new to him (Mr. Symonds) and which, he believed, from his experience, would shorten many difficult and even dangerous operations. There were two aspects of the question Mr. Kellock had brought before them: the first, and most important, being the treatment of long-standing cases. Where the process of disease had extended beyond the kidney along the vessels, they all knew what immense difficulty there sometimes was, in operations, in removing the kidney. He had had a fair experience of such operations and could only recall one in which he had failed to get out the kidney, the patient in that case dying. He believed that that patient might have survived if the operation suggested by Mr. Kellock had been performed. The second point referred to by Mr. Kellock had been the ligaturing of the vessels. He (Mr. Symonds) had had some experience of operating on the kidney from the front. They would remember that in the history of the subject Knowsley Thornton advocated operating from the front, which was opposed to that of Sir Henry Morris who advocated the lumbar method. A good deal of discussion had taken place at that time as to which was the better method, and he (Mr. Symonds) had employed both methods, removing from the front both tuberculous and cystic kidneys. He certainly had found that was an operation which gave no particular difficulty; and even in tuberculous cases he had not met with disaster, although he had encountered difficulty in dealing with the pedicle where there was a great deal of fibrous material round it. From his own attempts to remove kidneys from the front, he would not anticipate much difficulty in ligaturing the vessels from the front. He thought, however, Mr. Kellock's case must have been more than usually difficult, and that was no doubt explained by the existence of the sinus. From his experience of tuberculous and cystic cases he did not think they would find the actual application of the ligature difficult in the majority of cases.

Mr. JOCELYN SWAN thought all who had had experience of such cases would agree that the operation suggested by Mr. Kellock was certainly one of value in very difficult cases. If Mr. Kellock in the case in question had been obliged to remove the kidney by the usual methods from the loin, that would have been difficult owing to the amount of cicatrization, and they all realized the difficulties one might meet with in doing a subcapsular operation. He took it, therefore, that the case reported by Mr. Kellock was an important one which might help in the future in deciding whether subcapsular nephrectomy or renal ligation should be performed. However, Mr. Swan was of opinion that the cases suitable for the operation described by Mr. Kellock would be few and far between. He could hardly comprehend that

the operation would be an ordinary one unless there were some sinus, or opening, already made, because he did not think the mere tying of the renal vessels would do any good where there was suppuration, e.g., of a tuberculous nature, draining away through the ureter, without the removal of the septic focus.

The PRESIDENT (Mr. G. H. Makins, C.B.) said the first time he ever heard of the renal artery being tied as a substitute for nephrectomy was by Sir William Bennett. This was in a case of rupture, and the renal artery was tied as a substitute for removing the kidney, although, he believed, the kidney was afterwards removed. With regard to the case spoken of by Mr. Kellock, it was reading of that which had induced him (the President) to perform this operation. The failure of it was due to the local difficulties met with. The case was a very unusual one, an appendix abscess involving the ureter. After the appendix abscess was opened urine flowed very freely through the wound. At the time little was thought of that, as it was assumed the communication was with the bladder, but as the fistula persisted, the patient's bladder was examined and it became clear that the urine came from the ureter. The man went through a long chapter of accidents, suppuration tracking along the course of the ureter and round the kidney. An exploration to find the opening in the ureter failed on account of the induration of the retroperitoneal tissue. The patient got better at the time, but the urinary fistula persisting, it was eventually decided to remove the patient's kidney. The loin was opened with this intention, but the induration around the kidney was such that the operation was given up. Two or three weeks later an incision was made at the outer margin of the right rectus, and the hilus of the kidney exposed from the front. The same difficulty was then experienced which had been described by Mr. Kellock, the tissue around the pedicle of the kidney was just as hard as that which had been found in the loin, and separation of the renal vessels was impossible, hence the pedicle was tied *en masse*. The immediate result of the operation was to reduce the escape from the fistula almost to nothing, but in a few weeks' time the amount steadily increased, and finally the patient had the same trouble as before. That might have been due to failure to include the whole arterial supply, or possibly a supplemental artery was present. The operation had only had a temporary effect, and finally the twelfth rib was resected and a subcapsular nephrectomy was completed.

Mr. FRANK KIDD said he would like to call attention to a method of exposing the kidney by the lumbar route brought forward by William J. Mayo.<sup>1</sup> The patient was placed prone on an Edebohl's cushion and the incision commenced as a vertical cut 3 in. long, crossing the neck of the twelfth rib and parallel to the spinous processes. The incision opened up the sheath of the erector spinæ muscle, and was then carried downwards and forwards through the muscles parallel to the outer edge of the quadratus lumborum to within

<sup>1</sup> *Annals of Surgery*, Philad., 1912, lv, p. 63.

an inch of the crest of the ilium. By pulling inwards the erector spinæ the quadratus lumborum and the external arcuate ligaments were exposed and cut through, by which means the twelfth rib was freed from its main attachments and could be dislocated upwards. This gave direct access to the vascular pedicle of the kidney, and made the application of the ligature a comparatively easy matter even in cases of densely adherent pyonephrosis. He had made use of this method in cases of pyonephrosis and had found that it overcame the chief difficulty of the operation—namely, proper access to the pedicle. Had it been used in Mr. Kellock's case not only could the ligature have been more easily applied to the pedicle but there would have been no need to leave the kidney to come away in sloughed-off fragments. Such an incision would also obviate the great objection to Mr. Kellock's method—namely, the exposure of a pyonephrosis across the intact peritoneal cavity, with its added risk of causing general peritonitis. He was very much struck that no mention had been made in this case of any attempt to estimate the functional value of the other kidney by means of catheterization of the ureters, and the examination of the separated urines, before resorting to the serious step of putting an end to the existence of one kidney. He was strongly of the opinion that no operation (save nephrotomy in urgent cases) should be performed in a case of pyonephrosis until such tests had been applied.

MR. KELLOCK, in answer to the question as to whether the vessels were found thrombosed, said that the alarming hæmorrhage that took place when he touched the stone was good evidence that the artery at any rate was patent; he could not speak for certain as to the condition of the vein, but he did not think it was thrombosed. The ligature was placed fairly close to the aorta. In answer to Mr. Swan, he said that the reason why he had not tried to remove the kidney in the ordinary way was because he feared to touch it on account of the previous hæmorrhage. Of course the operation was not universally adaptable. In dealing with a tuberculous kidney, excision through the loin in the ordinary way might suffice, but it remained to be seen what an operation such as he had brought before them would do in the case of an aseptic tuberculous kidney. In the case mentioned by the President, Mr. Kellock thought that collateral circulation might have been set up in the kidney, either from an aberrant artery or one coming from the suprarenal. With regard to the situation of the incision, the one he had made he considered the best for getting at the pedicle. It was true one might get more room by the other method, but as far as getting at the pedicle was concerned the incision he had used answered all purposes. It depended on whether there was a tumour in the kidney, or whether the kidney was of normal size; the situation of the incision could be a matter of choice in individual cases. Mr. Kellock said he had made up his mind that the other kidney was acting, and the immediate effect of the operation showed that when stress was thrown on it, it was quite equal to its work.



**Three Unusual Cases of Renal Tumour, with a Discussion of the Operative Treatment of the Condition.**

By J. SWIFT JOLY, F.R.C.S.

My only reason for bringing these cases before your notice is that they appear somewhat interesting from the clinical point of view. Although the pathology of renal tumours is a subject of absorbing interest I do not propose to touch on it in this paper. My remarks are entirely confined to recording some unusual clinical observations, and to discussing the operative treatment of these tumours.

CASE I.

J. K., male, aged 53, was sent to me at St. Peter's Hospital on October 17, 1910, by Dr. Chepmell. Three months before this date the patient had rather a sharp attack of pain in the left loin. This was accompanied by vomiting, and lasted about an hour and a half. Immediately afterwards he passed a large quantity of blood in his urine; the next time he made water it was tinged with blood; later in the day the urine was clear. A fortnight later he had a similar attack. Two months after this he had a third attack of pain; this time, however, the pain spread down to his groin and into his testicle, and he passed several clots in addition to the fluid blood. Besides these painful attacks the patient had seven or eight painless attacks of hæmaturia. They came on without obvious cause, and lasted for periods varying from a couple of hours to two or three days. In other respects he felt perfectly well.

Examination: The urine was clear, acid, contained no albumin or sugar; no deposit. The left kidney was slightly tender on palpation; it was displaced downwards, and about half of it could be felt under the costal margin. This part of the organ appeared normal in size and shape. On full inspiration, however, it was just possible to feel an irregularity of the kidney close up under the ribs. The kidney moved with respiration, but could not be replaced in its normal position under the ribs. The right kidney could not be felt.

Cystoscopy: The bladder was normal. The right ureter was normal and the efflux copious and clear. From the orifice of the left ureter a wormlike mass was seen projecting. It was of a grey colour and stippled with black spots (? hæmorrhages). The free end was capped with mucus. The mass appeared to be about  $\frac{1}{4}$  in. in diameter, and



projected nearly  $\frac{1}{2}$  in. into the bladder. The ureter was contracting frequently and violently, and at each contraction the mass was partially forced out into the bladder, but when the contraction passed off it resumed its original position. No urine was seen issuing from this ureter.

The X-ray examination was negative to calculus.

A week later the patient was again cystoscoped. The mass had disappeared. The left ureteric orifice was round and slightly dilated, and clear urine was seen coming from it. The ureters were catheterized, and the urines from the two kidneys separated. Duration three hours.

|                  |     |     |     | Right kidney  |     | Left kidney   |
|------------------|-----|-----|-----|---------------|-----|---------------|
| Quantity         | ... | ... | ... | 6 oz.         | ... | 4 oz.         |
| Specific gravity | ... | ... | ... | 1015          | ... | 1007          |
| Urea             | ... | ... | ... | 1.7 per cent. | ... | 0.7 per cent. |

Operation, November 11, 1910: The oblique lumbar incision was made use of, but it was prolonged farther forward than usual so as to give freer access to the kidney. As soon as the perirenal fat was exposed the kidney was palpated through it, and a large irregular tumour felt at its upper pole. The kidney was removed enclosed in its fatty capsule, the ureter having been divided at the brim of the pelvis. The wound was closed in the usual manner.

The patient had an uninterrupted convalescence. Since the operation he has been in perfect health and has been doing his ordinary work. I saw him on March 3, 1913, nearly two years and four months after the operation. No signs of a recurrence can be made out by clinical examination.

Examination of the specimen: As soon as the fatty capsule was stripped off, it was found that the lower two-thirds of the kidney was normal to the naked eye. From the upper pole sprang a nodular rounded tumour; it was about the size of a billiard ball. The perirenal fat was adherent to the tumour. The ureter was normal, but the pelvis of the kidney was distended with a soft mass, which showed no tendency to invade the ureter.

On section the tumour presented the usual naked-eye appearances of a hypernephroma. The growth had replaced the upper pole of the kidney, and from it a downgrowth had invaded the renal pelvis and filled it completely. Although it had become moulded to the shape of the pelvis it was nowhere adherent to it. The lower part of this downgrowth had exactly the appearance of the fragment I saw protruding from the ureteric orifice.

Microscopically the tumour was a hypernephroma.

To my mind the most unusual feature of this case is the observation of the fragment of tumour projecting from the ureteric orifice. I have not been able to find a similar observation recorded in the literature. It is by no means uncommon to see long thin clots emerging from the ureters, but this fragment was quite unlike any clot. Cases are on record in which the growth has grafted itself on to the ureter near the vesical orifice, and this graft projected into the bladder. In my case I think this may be excluded as the patient has not had any recurrence at the ureteric orifice.

#### CASE II.

G. H., male, aged 55, was sent to me at St. Peter's Hospital by Dr. Chambre, of Ealing. He was first seen on April 29, 1912. The patient had two attacks of hæmaturia, one four weeks and the other two before this date. They lasted about a day each, and came on without obvious cause. On both occasions he passed clots, one of which was long and thin, "like a piece of fine string." During the attacks he had some difficulty of micturition. This was due to the clots. Patient had been quite free from pain. He stated that he had lost flesh lately.

Examination: Urine clear, acid, free from albumin and sugar; no deposit. The right kidney was enlarged to about twice its normal size. The enlargement was most marked at the lower pole. The kidney was hard and irregular, it was painless on palpation, and moved freely with respiration. The left kidney was not palpable.

Cystoscopy: Bladder normal. Clear effluxes seen from both ureters; however, that from the right was not so frequent or as copious as that from the left.

A week later he returned to the out-patient department saying that he had another attack of hæmaturia on his return home after the last examination. This time the tumour was again palpated. Immediately afterwards he passed some bloody urine. He was then cystoscoped, and a long, wormlike clot was seen extruding itself from the right ureter. Patient was advised to come into the hospital for operation, but refused to do so.

Late at night on July 11 this patient was admitted into the hospital with retention. He stated that he had had several attacks of hæmaturia since he was seen in the out-patient department, and that a very severe one came on that morning. He had been unable to pass water for about eight hours. His bladder was distended, and reached to within an inch of the umbilicus. A Bigelow's evacuator was passed and the bladder

emptied of clots. The next day the hæmorrhage abated somewhat and he was able to pass his water naturally; the next few days there was practically no bleeding. However, on July 15 it recommenced, and his bladder again became filled with clots. The next day clots had to be washed out of his bladder twice, and the following day he was still bleeding. As the patient was feeling the loss of blood I decided to operate at once.

Operation: A long oblique lumbar incision was made, and the perirenal fat rapidly exposed. It was very difficult to separate this from the peritoneum, as large vessels were coursing through it. Eventually the pedicle was reached and tied, and the kidney removed in its fatty capsule. The suprarenal was also removed, but one of its vessels gave rise to troublesome hæmorrhage till it was caught and ligatured. The peritoneum, which was torn in removing the tumour, was now sutured and the wound closed.

The patient was very much collapsed after the operation. In spite of infusion of saline and free stimulation he grew progressively weaker and died the same night. No post-mortem examination was allowed.

Examination of the tumour: When the kidney was split open it was found that the tumour was a hypernephroma which originated in the lower pole. Secondary growths were scattered throughout the renal substance, and several were projecting into the pelvis or calyces. It was not possible to determine which of these caused the hæmorrhage. One small nodule of growth was found in the perirenal fat.

It has been stated that hypernephromata do not as a rule give rise to serious hæmorrhage, and that even if the bleeding is severe it is remarkable how slight are the symptoms attributable to this cause. This case refutes both these statements. I have never seen such profuse or uncontrollable hæmorrhage from any other renal condition. It is also unusual that hæmaturia can be induced by the mere palpation of the kidney, but an examination of the specimen shows how easy it would be to cause a slight abrasion of one of the nodules that projected into the renal pelvis.

### CASE III.

J. C., male, aged 44, was sent to me at St. Peter's Hospital by Dr. Reynolds, of Watford. He stated that five years previously he noticed some blood in the urine. This lasted for two or three days and then ceased. Six months later he had another attack. He was then

free from all symptoms for about a year, when a third attack came on. Two years after this he had another similar bout of bleeding, and three months ago yet another. These attacks came on suddenly, and were painless, except when clots were present in the urine. Then a dull ache was felt in the left kidney region. Usually they lasted about three or four days, and then the urine gradually became clear. The patient had had malaria.

Examination: Patient was a stout, well-nourished man. Urine clear, acid, contained a trace of albumin, no sugar; slight deposit of red blood cells. No crystals or casts were seen. A large, hard, smooth mass could be felt in the left hypochondrium, and extending down into the left lumbar region. The upper limit of this tumour could not be felt as it extended upwards under the costal margin. The tumour filled up the loin. It was painless on palpation, moved freely with respiration, and was dull on percussion. No fluctuation could be made out in the mass. The left kidney could not be palpated apart from the tumour. The right kidney was not palpable. Patient had a slight varicocele.

Cystoscopy: The bladder was normal except for a slight amount of trabeculation. The right ureter was somewhat dilated and round. The efflux was clear and frequent. The left ureteric orifice was smaller than the right. It was round and slightly oedematous. Only one very small turbid efflux was seen.

Catheterization of the ureters: The left ureter was catheterized. When the point of the instrument reached the renal pelvis a gush of turbid fluid escaped from the ureter beside it. Though the catheter was left in situ for three hours not a drop came through it. This was not due to blocking the catheter, but to the fact that the kidney was not secreting.

Operation (June 16, 1911): An incision about 5 in. long was made parallel to and immediately outside the left linea semilunaris. The centre of this incision was on a level with the umbilicus. The abdomen was opened, great care being taken of the nerves which were retracted upwards and downwards. The tumour was palpated, and proved to be renal in origin. The peritoneum over it was normal. The region of the pedicle was carefully palpated; it appeared to be free from induration, and the renal vein was evidently not filled with clot or an extension of the growth. No enlarged glands were felt along the course of the aorta. Finally, the under-surface of the liver was examined, but it appeared normal. As it was thought that the tumour could be removed, the peritoneum was closed, and a high cushion placed under the left

lumbar region. A long incision was made from the centre of the first one outwards and slightly upwards to a point about an inch below and in front of the tip of the last rib. The peritoneum was exposed in the anterior part of this incision and the perirenal fat in the posterior. The peritoneum was then raised from the front of the tumour and retracted inwards towards the middle line. Next the hand was insinuated behind the fatty capsule, which was separated from the muscles of the lumbar fossa. This part of the operation was rendered tedious by the number of vessels which needed clamping. Finally the kidney (enclosed in its fatty capsule) was completely freed from all its connexions except those on its inner aspect. The ureter was divided just above the brim of the pelvis. The tumour was retracted strongly outwards and the tissues separated from the side of the aorta. This dissection was made from below upwards. It was rendered difficult on account of the size of the tumour, which had come to lie very close to the side of the vessel. When the renal pedicle was reached it was clamped and divided, as were also the capsular vessels. The tumour, which was now completely free, was lifted out of the lumbar fossa and removed. As the patient was now feeling the effects of the prolonged operation, a pint of saline was infused into his median basilic vein, and the wound packed with towels wrung out of hot saline, while the numerous vessels were being tied and the muscles sutured.

Patient rapidly recovered from the shock of the operation, and had an uneventful convalescence. Since the operation patient has been perfectly well, and has gained over 4 st. in weight. His abdominal wall is very firm in spite of the strain that has been put upon it. I saw him on March 3, almost a year and nine months after the operation, and was unable to detect any evidence of a recurrence.

Examination of the specimen: When the tumour was removed it looked like a huge ball of fat, considerably larger than a coconut, no portion of the kidney itself being visible. It weighed  $3\frac{3}{4}$  lb.; nearly half of this weight was due to the perirenal fat, which was about  $\frac{1}{2}$  in. in thickness. Four lymphatic glands were found in it, they were not enlarged, and to the naked eye were not involved in the growth. When the fat was removed the kidney was seen to have lost its characteristic shape, and to have become ovoid. It was covered with nodules where the growth had all but broken through the renal capsule.

On section it was seen that the new growth was centrally placed. It had displaced the secreting tissue of the kidney till the latter appeared only as a thin capsule surrounding the mass. The tumour had protruded

itself into the renal pelvis, but had not ulcerated into it. The result was that the cavity of the pelvis was reduced to a narrow slit. On section it was seen that bands of fibrous tissue had divided the mass into islands of greyish-white tissue; into several of these hæmorrhage had taken place, and many small degeneration cysts were to be seen.

Microscopically the tumour was a primary carcinoma.

#### DISCUSSION OF THE OPERATIVE TREATMENT.

In planning an operation for the relief of a renal tumour, the surgeon is met by the difficulty that he must not only remove the tumour, but remove it in such a manner that the recurrence—at least a local recurrence—should be rendered as remote a contingency as possible. To attain this end one must be able to diagnose the condition in its early stages and then do as extensive an operation as the anatomical relations of the parts allow.

In these remarks I shall confine myself to the question of operation, but as this largely depends on the state of the tumour and the patient's condition, I am forced to say a few words on the early diagnosis of renal growths. In my remarks I shall confine myself entirely to malignant tumours of the kidney occurring in adult life.

The following operations have been advocated and performed for this condition: (1) Partial nephrectomy. (2) Simple nephrectomy. (3) Simple nephrectomy followed by removal of the perirenal fatty tissue. (4) Removal of the kidney enclosed in its fatty envelope; this involves removal of the suprarenal capsule. (5) Removal of the kidney, perirenal tissues, suprarenal capsule, and the lymphatic vessels and glands all in one mass.

(1) A partial nephrectomy is contra-indicated if the tumour is definitely malignant, even if it be small enough to permit of this operation being performed. Such minute tumours rarely give rise to symptoms, therefore they are only met with when the kidney is explored for some other cause. If a small tumour of doubtful malignancy is found, one is justified in doing a partial nephrectomy provided that a more extensive operation is subsequently performed if the growth proves to be malignant on microscopic examination.

(2) By the term "simple nephrectomy" I mean nephrectomy as performed for non-malignant diseases of the kidney. If the diagnosis of tumour is made from clinical observation, and the surgeon approaches



the operation with the full knowledge that he is dealing with a case of malignant disease of the kidney, then a simple nephrectomy is contra-indicated. The operation is not extensive enough to hold out any hope that the patient will gain more than temporary benefit from it. The reason of this is not far to seek. The kidney is such a small organ that no tumour of the parenchyma can exceed the size of a walnut without causing a visible projection on its surface. But as most renal growths appear to have their origin close under the capsule, they may form a projection on the surface of the kidney long before they reach this size. If such a projection is examined, it will be found that the tumour cells are in actual contact with the fibrous capsule of the kidney. Although this forms a barrier which for a time limits the extension of the growth, it becomes progressively thinner and thinner and is finally ruptured. Long before this happens, however, a chronic localized perinephritis is set up by which the fatty envelope becomes sclerosed and adherent to the altered portion of the kidney. These adhesions are at first fibrous, later on they may become infiltrated with tumour cells, although no macroscopic breach of the capsule can be found. Now, if one attempts to do a simple nephrectomy in one of these cases, the possibility of rupturing the capsule when enucleating the kidney from its bed is obvious. The capsule will tear far more readily than the adhesions, and once it is torn the tumour cells are scattered over the wound. This is an accident that may happen to the most careful operator, and is one that practically dooms the patient to an early recurrence. Again, there is a moderately free anastomosis between the lymphatics of the renal cortex and those of the fatty capsule. Along these the tumour cells may spread, and the growth may graft itself on to the perirenal fat. In one of the cases I brought to your notice to-day a nodule of growth was found in the perirenal fat. It was quite isolated from the kidney, and would certainly have been left behind if a simple nephrectomy had been done. Whether this is a common occurrence or not I am unable to say, as the fatty capsule has not, as a rule, been carefully examined for these nodules. In any case, the fact that nodules of growth do occur in this situation forms the very strongest argument against the operation of simple nephrectomy. These objections hold equally good against all methods of doing the operation.

(3) Simple nephrectomy with subsequent removal of the perirenal fatty tissue: This operation is practised by many men of repute, and has been recommended by Albarran as the method of choice. This appears



strange to me, for not only was Albarran fully aware of the risk of tearing the fibrous capsule when enucleating the kidney, but he even describes the more radical method of Grégoire. To remove a malignant tumour and afterwards to dissect out piecemeal the surrounding tissues, lymphatics, and glands, is considered bad surgery if done for cancer of other organs. Why, then, should it be the correct method of dealing with cancer of the kidney? It seems to me that the second stage of this operation is an attempt to atone for the faults of the first. But why commit these faults? I can only imagine one condition which would call for this operation. That is, if a surgeon removed a malignant kidney under the impression that he was dealing with a non-malignant disease. He ought then to complete the operation and endeavour in this way to rectify his error of diagnosis.

(4) Removal of the kidney within its fatty capsule: In performing this operation the aim of the surgeon is to remove the kidney as it lies enclosed in its fatty capsule without disturbing the relationship of the parts. This means that, except in very thin patients, the kidney is not seen until the specimen is examined after the operation. Again, as the suprarenal capsule is enclosed within the perirenal fat, it must be removed with the kidney. Although the removal of one suprarenal capsule seems to be a highly fatal operation in the case of some of the lower animals the reverse is the case in the human species. My cases presented no symptoms that could be referred to it, and I am unaware of any records in which such symptoms are mentioned. Removal of the suprarenal capsule adds somewhat to the difficulty of the operation. Its vessels are difficult to control as they are very short and are situated so high up under the diaphragm. Though I believe the complete operation should be performed as a matter of choice in cases of renal tumour, I feel that this procedure has a distinct place in the surgery of the condition. It is suitable for cases that will not stand the shock of a prolonged dissection of the juxta-aortic glands.

(5) The "complete operation," having for its object the extirpation of the kidney, the surrounding fatty tissues, the suprarenal capsule, and the lymphatic glands all in one mass, has been carefully worked out by Grégoire. To him belongs the credit of placing it on a definite and scientific basis. Before describing this operation let me remind you that the lymphatics of the kidney leave the organ at the hilum, and, coursing through the perirenal fatty tissue, end in the juxta-aortic glands. On the right side these glands lie on the anterior

surface of the vena cava, on the left they are to be found just to the left of the aorta. On both sides the whole chain from the pillars of the diaphragm to the bifurcation of the great vessels receive the renal lymphatics, and must therefore be removed. However, those lying near the renal vessels receive the bulk of the renal lymph, and are the most important from our point of view. Owing to the close proximity of the receptaculum chyli, once the cancer cells pass beyond these glands there is no possibility of preventing a generalized infection. Again, the perirenal fat is enclosed in a fascial envelope. Posteriorly this is formed by Zuckerkandl's fascia, anteriorly it is thinner, and is called the fascia propria of the kidney. This lies immediately subjacent to the peritoneum, and passes across the middle line in front of the great vessels. These two layers of fascia unite above and to the outer side of the fatty capsule of the kidney. Below they become thin and are lost in the subperitoneal areolar tissue. The aim of the operator is to keep outside this fascial envelope, and if he does so he will find that as he separates it from the muscles of the lumbar fossa behind and from the peritoneum in front, he will have the kidney and suprarenal capsule with all the perirenal fatty tissue lying, as it were, within the folds of a broad mesentery which springs from the great vessels. At the lower end of this the ureter is divided, and as the root of this "mesentery" is dissected off the great vessels the juxta-aortic glands are removed with it. This naturally is the most difficult part of the operation.

Legueu, in his description of Grégoire's operation, advises that the dissection of the glands should be made from above downwards. I think it is much easier to do it from below upwards, and to ligate the renal vessels only when the pedicle is reached. If this is done the tumour can be lifted more and more out of the wound as the dissection proceeds, and one is not hampered by it during the most difficult part of the operation.

Before discussing the question of incision I feel I must say a very few words as to the diagnosis of renal tumours. The three cardinal signs of renal tumour are: hæmaturia, pain, and tumour. All these may be present when the patient is first seen, or any combination of two of them—e.g., tumour and hæmaturia, or pain and hæmaturia. Occasionally only one sign is to be found. Hæmaturia is, in the majority of cases, the symptom that causes the patient to consult his medical attendant, but examination often reveals the presence of a tumour which was previously unnoticed. The hæmorrhage comes on spontaneously, and in attacks which may last for a few hours or a couple of days. It is

generally profuse, and frequently ureteric clots are passed. In early cases the pain is often due to the hæmorrhage. It may be localized to the renal area when it is due to distension of the renal pelvis with blood, or it may take the form of a renal colic if clots are passed down the ureter. When present it is valuable as an indication of the side affected. Of course, the hæmaturia must be proved by means of the cystoscope to come from one kidney, and from one kidney only. Another function of the cystoscope is to exclude tumours or other conditions of the bladder that may give rise to hæmaturia, and perhaps simulate the signs of renal growth. For example, a vesical growth springing from the neighbourhood of one ureteric orifice may constrict that orifice and cause a hydronephrosis of the corresponding kidney. In this case the symptoms would be hæmaturia, pain in the lumbar region, and enlargement of that kidney. Apart from hæmaturia, pain is usually nothing more than a dull ache in the loin. Neuralgic pains spreading along the lower dorsal or upper lumbar nerves indicate that the condition is inoperable. The tumour presents the usual characters of a renal tumour, but if the growth is a small one and situated at the upper pole of the kidney, one may not be able to feel it, and palpation only reveals an apparently normal kidney lying at a slightly lower level than usual. Diminution of the excretory function of the affected kidney is generally noticed, and is a valuable secondary sign. As the tumour grows by replacing the kidney substance it follows that the excretory function of a malignant kidney varies inversely as the size of the tumour; the larger the kidney the less it secretes. Of course, this is only approximately so, and exceptions occur which diminish the value of this rule. Unfortunately, where it is most needed we gain but little information from this rule, for it is the small tumours that are the most difficult to diagnose, and in these the excretory function of the two kidneys is nearly the same. However, if a kidney in which no tumour is palpable is bleeding, the fact that it secretes as much or nearly as much as its fellow must not be considered a contra-indication to surgical exploration.

From this brief outline it will be seen that we have two classes of patients to deal with: (1) Cases of unilateral renal hæmaturia, where a renal growth is suspected, but cannot be diagnosed by clinical methods. (2) Cases in which the diagnosis is definitely made by clinical methods. In both these classes the operative treatment should commence with a thorough exploration of the parts, to prove the presence of a tumour in the first, and to determine whether it can be removed in the second. In the first class this exploration is directed towards

the kidney, therefore a lumbar incision is best for the purpose; in the second, one wishes to examine whether the growth has involved the glands or the peritoneum, whether metastases have occurred in the liver or other abdominal organs, and whether an extension of the growth lies in the renal vein. For this purpose an exploratory laparotomy is necessary.

Now the T-shaped incision I made use of in my third case answers either purpose excellently. If one wishes to examine the kidney, the horizontal or lumbar limb of the T is first made; if it is necessary to explore the abdomen, the vertical limb gives free access. In either case the exploration forms an integral part of the operation. This, I think, is the great advantage of the incision I made use of over that recommended by Grégoire.

Grégoire's incision consists of a vertical portion which runs from the tip of the eleventh rib to a point just behind the anterior superior spine of the ilium. From either end of this an incision is carried forward; one follows the costal margin, the other the crest of the ilium. The length of these two incisions depends on the size of the tumour. Thus a flap consisting of the whole thickness of the belly wall is turned forwards from the flank. This incision gives a very perfect exposure of the kidney and its pedicle, but is not well adapted for exploring the abdomen.

The oblique T-shaped incision gives nearly the same exposure as Grégoire's, as the vertical limb allows the lower part of the thoracic wall to be retracted upwards and outwards. In the future I hope to try a modification of this incision. I shall make the vertical limb higher up, so that the lumbar limb meets it at its lower end. In this case the incision will be shaped like an L on its side (┐).

In Grégoire's incision the lower intercostal nerves must be sacrificed, in the T-shaped incision this is not necessary. I retracted the nerves when exploring the abdomen through the vertical limb. The result was that in the operation the last dorsal alone was severed. If the tumour had not been so enormous I think I might have even avoided it. I do not think that this patient's abdominal wall would have stood the strain of his great and rapidly increasing obesity if I had made use of Grégoire's incision.

The results of operative interference with malignant tumours of the kidney are melancholy reading. Leguen states that 60 per cent. of cases have a recurrence within the first year, and that this recurrence almost always takes place in the scar. Observations on cases operated on at St. Peter's Hospital give the same result.

Rapid local recurrence after any operation for cancer is a sign that either the growth was attacked too late, when it was really inoperable, or that the operation was not wide enough. The difficulties that beset us in making the diagnosis of renal tumour only emphasize the necessity of an extensive operation. If a method such as Grégoire's, which allows a free removal of the perirenal tissues, comes into common vogue I feel confident that our results will be immeasurably superior to what they have been in the past.

#### DISCUSSION.

Mr. JOCELYN SWAN said that Mr. Joly had labelled his first two cases as hypernephromata, and the third case as a primary carcinoma. But looking at the specimen and noticing the hæmorrhage and areas of degeneration that had taken place, he (Mr. Swan) had little doubt that the third case also was a true hypernephroma and not a primary carcinoma. He had operated on eight cases of hypernephroma, and agreed that the one prominent symptom, as Mr. Joly had also stated, was painless hæmaturia. In Sir John Bland-Sutton's book the prominent symptom of hypernephroma was given as pain. With that he disagreed, and in nine of the cases he had had, six had commenced their symptoms with attacks of profuse hæmaturia in the kidney; therefore, in his experience, hæmaturia had been the common initial symptom of hypernephroma. With regard to the operations, Mr. Swan had himself practised what Mr. Joly had recommended—namely, the removal of the renal fatty capsule with the kidney, not separating it from the kidney—but he had not done the extensive operation of removing the glands as far as the bifurcation of the aorta. In one of his cases, upon which he operated in January, 1909, the patient was perfectly well. He had had other cases where the patients were still well after the operation, but not for so long a time. Some had recurred, not in the position of the lumbar wound, but in the lung or the liver. In one recent case, operated upon last October, a rapid recurrence had taken place in the crest of the ilium. He had explored it but could do nothing, and in six weeks there was a rapid recurrence in the liver. Another point he would like to mention was a difficulty which had occurred to him in the diagnosis of a renal tumour of the right side. In one case which had been under his care the patient had profuse hæmaturia from the right kidney, as shown by cystoscopic examination, but he was unable to feel the kidney because the anterior position of the liver was 3 in. below the normal, and he had very much doubt as to whether the man had metastases in the liver. He opened the abdomen, and saw the true condition of matters. There was a very large kidney affected by hypernephroma, which had grown upwards under the dome of the diaphragm, and had pushed the liver forwards and downwards, dislocating it as stated, and when, subsequently, he removed the kidney by the abdominal

operation it was impossible to feel the liver come down as it had done before. Mr. Joly had labelled his paper "Unusual Cases of Renal Tumour"; however, cases of hypernephroma formed 75 to 80 per cent. of cases of all renal tumours. Mr. Swan had had a case under his care which he was of opinion was unusual, and of which he showed a specimen. This was a kidney which he had removed from a youth, aged 18, suffering from very profuse hæmaturia, the most profuse hæmaturia he had ever seen. There had been bleeding for two days, and the patient was absolutely blanched, with a pulse about 120. Mr. Swan examined the patient through the cystoscope and saw bleeding from the right ureteric orifice. He explored the kidney, and it looked from the outside perfectly normal. He divided it right along the convex border, and just beside the pelvis of the kidney there was a tumour of about  $\frac{3}{4}$  in. diameter which was bleeding profusely. He removed the kidney. The patient did perfectly well, and had a rapid convalescence. The tumour was of a very vascular, spongy appearance, and microscopic section showed it to be a cavernous angioma. It was a distinct angiomatous tumour in the kidney, but not such as had been described by Mr. Fenwick as an angioma of a renal papilla.

Mr. FRANK KIDD remarked, in reference to Mr. Joly's first case, that he had seen a case of Mr. Hurry Fenwick's at the London Hospital, where the cystoscope revealed a mass of growth hanging out of the right ureteric orifice. The origin of this growth proved to be a stone in the pelvis of the right kidney, setting up a papillomatous carcinoma of the renal pelvis and secondary seedlings along the course of the right ureter. The condition mentioned by Mr. Joly was allied to those cases of hypernephroma met with from time to time in the post-mortem room, wherein a long pedunculated mass of growth was found protruding into the inferior vena cava, and even extending as far as the right auricle of the heart. He was under the impression that hypernephromata were of low malignancy so long as they remained imprisoned in their very definite capsules, but that when they burst out of their capsules they tended to advance rapidly, and if they burst into the renal vein death could not long be delayed. In Mr. Joly's case the growth seemed to have burst into the renal pelvis and thence to have escaped down the ureter, a fact which might influence the prognosis and render it more favourable. How large these tumours could become without giving rise to secondary deposits he had had a somewhat remarkable opportunity of proving. In August, 1911, he had explored the abdomen of a woman for what appeared to be an attack of peritonitis with localized abscess in the right loin. This proved to be a tumour the size of a cricket ball in the right lobe of the liver. As there appeared to be no evidence of a primary focus, he had excised a wedge-shaped portion of liver, leaving an inch or more of liver substance on either side of the tumour, and had brought the liver together by a special method of suture. Unfortunately, the woman died later of heat-stroke during the record heat of August, 1911, and a post-mortem examination was obtained. The wound in the liver had healed perfectly and no evidence could be found throughout the body of any other neoplastic deposit. Microscopic examination revealed that the



tumour resembled in every respect a Grawitz tumour, or hypernephroma of the kidney. It was therefore well worth while to make a determined attempt to remove the whole of the local growth, and he thought Mr. Joly had done so in these cases by including the perinephric fatty capsule in his dissection. Mr. Kidd added that Mr. Hurry Fenwick had been teaching for many years that painless hæmaturia was the cardinal sign of renal growth, and this was one of the reasons which rendered it so important that patients with painless hæmaturia should be cystoscoped directly they came up to the out-patient department with this symptom. Otherwise the opportunity was likely to be lost of determining which kidney was bleeding. He was much impressed with the indications as to which kidney was affected given by the functional tests applied to the separated urines when the hæmaturia was not present. He thought that this was a valuable diagnostic hint, and would bear it in mind for future use. With regard to the incision Mr. Joly had used, Mr. Kidd said that he had himself used such an incision, not only for the removal of large renal tumours, but also twice for the removal of large spleens. In every case it had healed up firmly and without giving rise to hernia. It was a form of incision that deserved to be more widely recognized as one not to be feared, especially if one were in a hurry to stop hæmorrhage, as, for instance, from torn splenic veins.

Mr. JOLY, in reply, agreed with Mr. Swan that the third tumour he had brought before them was very like a hypernephroma, but the diagnosis of primary carcinoma was made on the microscopic examination. There was a considerable amount of confusion as to the classification of these tumours. In Albarran's collection of cases about 30 per cent. were put down as hypernephromata. More recent statistics showed that hypernephromata formed about 75 per cent. of all renal tumours in the adult; therefore, Mr. Joly thought, Albarran must have classed as carcinomata or epitheliomata many tumours that were really hypernephromata. Of course, whether hypernephromata did arise from adrenal rests, or whether they did not, was still a subject for discussion. There were strong arguments for and against, and he did not think the matter could be considered as settled. Both Mr. Swan and Mr. Kidd had laid emphasis on the importance of hæmaturia as an early sign of renal tumour, and he entirely agreed with them. It was important that patients who passed blood in the urine should be cystoscoped both during an attack of hæmaturia and in the quiescent interval. If the hæmaturia was due to some kidney lesion one could only get information concerning it when the patient was examined during an attack. If the hæmorrhage was due to a bladder tumour one should cystoscope the patient when he was not bleeding, so as to be able to determine the size and position of the growth.



## **Surgical Section.**

May 6, 1913.

Mr. G. H. MAKINS, C.B., President of the Section, in the Chair.

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### **Obstruction of the Ureter by Aberrant Renal Vessels ; a Clinical Study of the Symptoms and Results of Operation.**

By J. HUTCHINSON, F.R.C.S.

It is natural to suppose that obstruction to the ureter by an aberrant vessel will develop if the kidney becomes abnormally mobile or floating, especially if the vessel runs in front of the ureter. But an analysis of the cases shows clearly that the obstructing artery is frequently found crossing the posterior aspect of the ureter (in Cases I, II, III, XI, XIII, XVIII, and XIX), as compared with five in front of the ureter (Cases I, IX, XVI, XX, and XXI). In ten cases the exact relative position is not noted. Moreover, in only a small minority was the kidney definitely floating.

We should therefore expect the obstruction to show itself at an early age, and inquiry into this point gives the following result: The onset of pain is always sudden and its date can be precisely fixed. In one case the attacks began at the age of 15, in one other there was a history of lumbar pain in childhood which may possibly have been due to this cause. But 15 to 25 years may be taken as the usual period of onset of symptoms: this includes fifteen out of twenty-two cases—i.e., quite two-thirds of the total number. In five cases the earliest sign of the trouble did not occur until the patient was aged over 30.

As regards the sex of the patient, there is a considerable preponderance of males—sixteen to only six females.

Fortunately the abnormality is almost always one-sided, and with regard to this the right kidney is involved nearly twice as frequently as the left. Reference will be made at the end of the paper to two

previously published fatal cases in which both ureters were obstructed by aberrant vessels.

To summarize the facts made out so far:—

(1) The abnormality, though a congenital one, rarely causes trouble in childhood until the period of adolescence is reached, sometimes not until middle life.

(2) The obstruction does not depend upon the kidney floating or becoming too mobile. Kinking of the ureter by the aberrant artery is produced in some other way than this. As is well known, floating kidney is frequent in women, rare in men.

(3) The aberrant artery is present much more often on the right side of the body than the left. It is occasionally present on both sides of the body, and has then even led to the patient's death.

Like all uncommon diseases, vascular obstruction of the ureter is not easily diagnosed, and it is not surprising to find that its subjects are apt to be treated for months or years under a completely mistaken diagnosis. Duodenal ulcer, gall-stone colic, appendicitis, and renal calculus are some of the conditions for which it is mistaken (supposing a cause to be assigned for the recurring attacks of pain), whilst in many cases no conclusion is arrived at by the physician for a long time. Cases III and XVIII are of peculiar interest: in them the patients were actually operated on for "floating kidney" without the real cause of their symptoms—the aberrant artery—being detected.

In Case IV the patient was the subject of attacks of pain through the long period of twenty-six years before resort to operation, then the kidney was disorganized and nephrectomy had to be performed. In Cases III, VII, and IX it was also found that the obstruction had lasted so long that relief was only possible by removal of the kidney. Apart from this there is a strong reason in favour of early diagnosis and operation—namely, the fact that the distended pelvis after a certain time cannot wholly recover even if the obstruction be removed. Hence sometimes the cure has not been complete, and recurrence of pain—doubtless owing to a valvular fold just where the renal pelvis passes into the ureter—has been observed. Owing to the difficulty of tracing patients for long it is impossible to say in what proportion this occurs, but I would especially draw attention to Case II, where after four years' complete freedom from attacks—following the operation—an isolated severe one was noted.<sup>1</sup>

<sup>1</sup> In Case XVII repeated attacks recurred after the operation and before the patient left the hospital.

To ensure an early diagnosis being made a close study of the symptoms must be of use, and sufficient material exists for the purpose. What positive and negative signs characterize vascular obstruction of the ureter?

(1) We have seen that the patients are generally males, that the pain is one-sided, on the right side twice as frequently as on the left, and that the first onset of the attacks occurs usually at the age of 15 to 25, and but rarely before this period.

(2) The attack of pain comes on as a rule independently of exertion and not infrequently when the patient is lying down. In Cases VI, XII, XIII, and XIV, however, it was noted that jolting or exercise favoured its occurrence.

(3) It has nothing whatever to do with the patient's diet, time of meals, constipation, &c. Neither aperients nor other medicines relieve it. These points help materially in the diagnosis from duodenal ulcer, appendicitis, and other intestinal conditions.

(4) The pain is exceedingly severe, doubling the patient up and making him sweat profusely. Vomiting frequently, but not always, occurs—e.g., Cases II, III, IV, V, VII, &c. The act of sickness relieves the pain.

(5) The pain is chiefly experienced in the lumbar region, but also in the front of the abdomen in some cases. It may radiate towards the groin and testis on the same side (Cases VIII and X), but this is exceptional as compared with the pain due to calculus. It is very rarely referred towards the shoulder as in biliary colic. It should be noted that the subjects are rarely of the age or sex in which gall-stones are met with. Moreover, relief is obtained by lying on the affected side (this is not invariably the case).

(6) There is a marked periodicity in the attacks, a fact difficult to explain. There is often an interval of months, perhaps even years, between the early ones. The later attacks will come on every week, or oftener. Finally, if the pelvis has dilated permanently the attacks practically cease, only a dull aching pain in the loin remains.

(7) With the exception of the cases just referred to, in which hydro-nephrosis has become established, there are no objective signs to be made out. The kidney is not felt to float. A moderate degree of distension of the renal pelvis cannot, of course, be detected on examination of the abdomen. The cystoscope *may* show congestion of the ureteric orifice on the affected side, but I think this observation too doubtful to be of value. A skiagram will, of course, settle the question

whether a renal calculus is present or not. In one case only of my series (Case XIII, under Mr. J. Sherren) the two conditions, calculi and aberrant lower artery, co-existed.

(8) As a rule, urinary symptoms are absent. There is no abnormal frequency of micturition during or after an attack, the urine is quite healthy. As exceptions, slight occasional hæmaturia, traces of albumin or pus, and pain in micturition have to be noted. But, contrary to what might be expected, decided interference with the urinary functions is conspicuous by its absence. Doubtless it is this fact that so often leads to delay in forming a right diagnosis.

Such is a picture of vascular obstruction of the ureter, and it will be found to be a consistent and uniform one, sufficiently so to justify exploration of the kidney from the loin in any case where these features are present. Now and then, as in one patient under my care, an aberrant artery may be suspected and yet proved not to exist; on the other hand, if the above conditions are present the surgeon may make his diagnosis with confidence and will probably find exactly what was sought for. The earlier the obstruction is relieved by operation the more complete will be the cure.

Now and then the surgeon will be led to explore from in front, especially if there is a suspicion that the vermiform appendix is in fault. This happened in two cases in my list, one of Mr. H. M. Rigby's and one of my own; in the former the appendix was found to be healthy, in the latter it was thickened; both were removed. In Case I, I was able to detect the dilated pelvis of the kidney and the band formed by the aberrant artery through the abdominal incision.

In the great majority of cases lumbar exploration alone is required; the artery and vein at fault (or perhaps an artery running by itself) are ligatured and excised. Fixation of the kidney should be performed provided it is too mobile or has been separated from its connexions.

The pelvis is sometimes distorted in an extraordinary manner, and a marked narrowing where it joins the ureter naturally suggests that a plastic operation should be performed. In one of the present series of cases (XIV) Mr. Hurry Fenwick did this, but as urine escaped from the wound for three weeks after the operation it may be doubted whether it was a perfect success. In another (Case III) Mr. Sherren incised the strictured part lengthwise and sutured the wound transversely (*see diagram*), but finding that the pelvis did not empty well

he performed nephrectomy. M. Peyrot<sup>1</sup> in a similar case performed uretero-pyelo-anastomosis. Suppuration followed with a urinary fistula which persisted a long time. I have not yet found record of a single case in which a plastic operation for this condition appears to have been followed by success. The variety of operations that have been devised for remedying a stricture or kink of the ureter is great, but I doubt if their success corresponds at all with their number. The continual passage of urine over the wound interferes so much with its proper healing that whether in the urethra or the ureter plastic surgery is disappointing in its results.

I believe in the case of vascular obstruction of the ureter, even though a marked narrowing has been produced where the aberrant artery crossed it, *it is best not to open the canal but to straighten out the pelvis and ureter as far as possible*, and to trust to Nature to do the rest.

The point of greatest importance is for the surgeon to operate early, before the pelvis has become dilated beyond prospect of recovery. The attacks of pain are so severe, and we may say typical, that it is surprising to find how long they are allowed to recur before surgical help is sought or given. It is quite exceptional—e.g., in Mr. Sherren's case (XV)—for the operation to be performed within a few months from the first onset of pain, usually several years are allowed to elapse. We can only explain this by the fact that the urinary symptoms are almost always absent, and also that a knowledge of the condition is not prevalent. Several of our text-books on surgery pass it over in silence, or mention it in the most cursory manner. A valuable paper by Dr. G. Newton Pitt<sup>2</sup> was one of the earliest in this country to draw attention to the subject. Dr. Pitt recorded four cases, derived from the post-mortem room, in which hydronephrosis was due to abnormal renal vessels. Two were in women and two in men, in three the left kidney was affected and in one the right, in all four the abnormality involved only one side, and in all four the abnormal vessel ran behind the ureter, which looped over and was kinked by it. It is curious that in three of the cases the vessel in fault was a vein, in only one an aberrant artery. It is obviously impossible to judge in Dr. Pitt's cases at what age the obstruction began, but two of his patients were only aged 17 and 23 at the time of death—when hydronephrosis was well marked.

<sup>1</sup> Bull. et mém. de la Soc. de Chir. de Par., 1904, p. 519.

<sup>2</sup> Trans. Path. Soc., 1894, xlv, p. 107.

Dr. Ekehorn, a Swedish surgeon, collected a series of published cases in a paper published in 1907.<sup>1</sup> He narrated very fully one case of his own, together with twenty-four from various sources. Sixteen only out of the twenty-five are narrated with sufficient detail to be of use. Dr. Ekehorn's list does not bear out the preponderance of male subjects shown in mine; thus there were eleven females to five males. Moreover, the sides affected were in nearly equal proportion. In two cases the attacks of pain started in childhood, at the age respectively of 2 and 7 years.

I have preferred to leave the deductions from the London Hospital series unaltered, and I have to thank my colleagues, Messrs. F. H. Fenwick, H. M. Rigby, J. Sherren, Hugh Lett, Russell Howard, and Milne, most heartily for allowing me to utilize the notes of their cases. These were taken from the hospital records between 1904 and 1912.

In none of the twenty-one cases I have brought forward was there any reason to believe that both kidneys possessed an aberrant artery which could cause obstruction, the symptoms in all were one-sided only. But I have found records of two published cases in which, unfortunately for the patient, the abnormality existed in both kidneys. Hamilton<sup>2</sup> performed nephrectomy on the left kidney of a young man, aged 22, who had suffered for three years from recurrent attacks of left-sided pain, and who presented a tumour in the left loin (hydronephrosis). On the third day after the operation anuria was evident and the patient died on the fourth. The right ureter was found to be obstructed by a small abnormal artery and vein going to the lower pole of the kidney. The cause of the trouble in the left kidney had not been made out at the time of operation, but dissection of the specimen now showed that a precisely similar condition existed on that side. Roberts<sup>3</sup> reported the case of a young man who from the early age of 2 years until his death at 20 suffered from recurrent attacks of pain in both loins, with signs of double hydronephrosis. He died of suppression of urine. A drawing is given of the left kidney, the pelvis of which is much dilated owing to obstruction of the ureter by an aberrant artery, and presumably the same condition was present on the other side.

<sup>1</sup> *Arch. f. klin. Chir.*, Berl., 1907, lxxxii, p. 955.

<sup>2</sup> *Glasgow Med. Journ.*, 1904, lxi, p. 120.

<sup>3</sup> *Brit. Med. Journ.*, 1868, i, pp. 582, 605.

*Case I.*—Intermittent attacks of right hypochondriac and lumbar pain for four years. Anterior abdominal exploration, vermiform appendix (thickened) removed, hydronephrosis detected, due to aberrant artery. Lumbar incision, artery divided. Subsequent slight recurrence of pain.

E. H., a fish porter, became subject, at the age of 20, to attacks of "gnawing pain" in the right side of the abdomen, both front and back. These attacks came on suddenly, and were independent of diet or of exertion: they

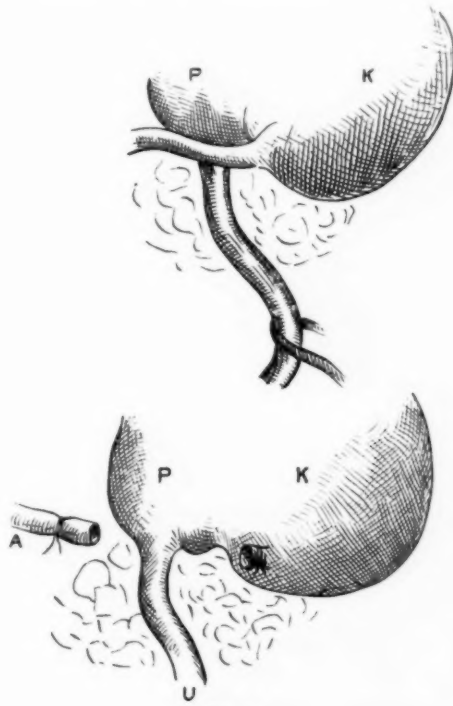


FIG. 1.

Large aberrant artery crossing behind ureter, causing dilatation of the pelvis (P).  
The lower figure shows the effect of resection of the vessel. (Case I.)

came on at intervals of a few months and would last about a day. No medicine relieved him. He was for some time in St. Mary's and the London Hospitals, where careful examination by X-rays and bismuth meals, &c., failed to elicit any cause for the attacks. His urine was always normal, there was no frequency of micturition. Dr. Frederick Green, of Old Burlington Street, brought the patient to me in June, 1912; the attacks then came on every week.



I made a provisional diagnosis of obstruction to the right ureter by abnormal artery, but decided to explore the abdomen from in front. By a curious coincidence one of his sisters had been treated for appendicitis and renal calculus. Laparotomy was performed at the outer border of the right rectus; the region of the gall-bladder showed a band of peritoneum (no doubt congenital), passing over the duodenum from the gall-bladder to the colon; this was completely divided. The vermiform appendix was next exposed and found to be thickened; it contained three faecal concretions. The appendix was removed, but I did not feel satisfied that the cause of his attacks had yet been discovered. The right kidney was normal as to its mobility. The pelvis was dilated to nearly the size of a cricket ball; just below this a band was felt to run transversely. The anterior wound being closed, the patient was turned on to his left side, and the right kidney exposed from behind. A large aberrant artery and vein were seen to cross behind the ureter to the lower pole of the kidney (fig. 1). When these were excised between ligatures the dilated and tense pelvis contracted a good deal but not entirely. Two kangaroo tendons were used to anchor the kidney to the muscles and the wound was closed. He was soon well, but about a month later Dr. Green brought him to me again on account of recurrence of pain. This, however, passed off, and nine months later Dr. Green reported that the patient was perfectly well and had been free from pain for a long time. The case is of particular interest, since two other abdominal conditions were found by laparotomy which might wrongly have been supposed to give rise to the attacks of pain.

*Case II.*—Intermittent attacks of left lumbar pain for two years. Exploration of left kidney, abnormal artery found at *either pole*, the lower one passing below the ureter, and causing distension of the pelvis. Division of the vessel; fixation of the kidney. After four years complete relief—one isolated recurrence of pain.

W. E., at the age of 15, after an abdominal strain, was seized with a sharp attack of pain. This was followed by similar attacks every week, and later they became still more frequent, every two or three days. They usually came on gradually, and were eased by his lying on the affected side. Sometimes he was sick, but never fainted. No cause could be arrived at and no treatment was of avail. After suffering from the attacks for two years he came under the care of my colleague, Dr. Wilfred Hadley, who transferred him to me. There were no abnormal physical signs, and the urine was healthy, but as the pain was definitely renal I decided to explore the kidney. The pelvis was found to be dilated, owing to an aberrant artery which passed behind the ureter and kinked it (fig. 2). The vessel was divided between ligatures; the pelvis emptied itself when the obstructing cause was removed. A similar aberrant artery ran above the pelvis to the upper renal pole. The kidney was fixed by kangaroo tendon sutures to the muscles, but it was not really floating. Next day he had an epileptic fit (the first he had ever had), but otherwise he made an excellent recovery. For four years the relief from pain was complete, then a

sharp attack came on whilst he was dancing. The pain was as before in the left loin, and was so severe as to make him actually vomit. Under treatment with aspirin and hot baths he recovered and has been quite well since. He can take active exercise freely. The occurrence of abnormal arteries entering both poles of the kidney is noted in one or two more cases. The upper artery has but little pathological or practical importance, as it can only obstruct the outflow of urine if the pelvis be placed unusually high (*see Case XI*).

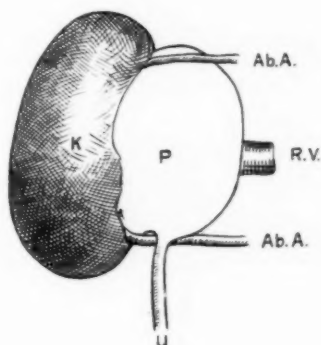


FIG. 2.

Aberrant artery crossing behind the ureter. A similar vessel runs to the upper pole. R.V., renal vessels. (*Case II.*)

*Case III.*—Left hydro-nephrosis due to kinking and obstruction of ureter by aberrant artery. Operation for movable kidney (without relief). Causal condition not found. Subsequent operation. Ureteroplasty attempted, but found to be unsatisfactory. Nephrectomy.

J. B., a soldier, when a boy attended Guy's Hospital for attacks of pain and sickness, which were relieved by treatment.<sup>1</sup> His present trouble started about the age of 20 when he was serving in the Army. Attacks of pain well localized in the back and left loin came on independently of taking food or of exercise. The pain was relieved by local warmth or by vomiting; each attack would last some twenty-four hours. There were no urinary symptoms. He was operated on at Aldershot for supposed floating kidney, and obviously the aberrant artery was not then detected. No relief followed the operation; the attacks of pain continued to occur at intervals of two weeks to four months, the pain being felt in the left loin and then radiating forward to the hypochondrium about the

<sup>1</sup> He thought these attacks were like those which came on in adult life. He attended Guy's Hospital between the ages of 3 and 8; circumcision was done and was supposed to have cured him. Anyhow, he had twelve years' respite from attacks of pain.

ninth rib cartilage, and nowhere else. The onset was usually about 8 p.m., but frequently would wake him about 4 a.m. Vomiting was practically constant after the pain had lasted two or three hours, and as usual in these cases it relieved. There was never any hæmatemesis or melæna: on the other hand, there were no urinary symptoms of any kind—except the doubtful one that he passed no urine during an attack but an excessive amount (? a pint) just afterwards. He was admitted under Mr. James Sherren, who examined him with the cystoscope and found nothing abnormal: a catheter would not ascend more than about 4 in. of the left ureter, but this must have been some accidental hitch, as the stricture was subsequently found 10 in. above this level. Nothing abnormal could be felt in the abdomen, the left kidney was not floating, there was a long scar in the loin due to the previous operation performed at Aldershot. The kidney was exposed from behind, and after some difficulty, owing to the method of fixation previously employed, it was brought into the

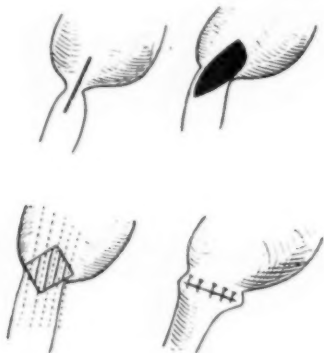


FIG. 3.

Attempted plastic operation on the ureter. (Case III.)

wound. The pelvis was greatly dilated, the kidney enlarged and rather soft. An aberrant renal artery was found passing behind the ureter, producing a stricture in the latter "which almost occluded it." This artery was divided between two ligatures. The ureter was opened and a ureteric bougie passed down to the bladder: no obstruction was found in the lower part. A careful attempt was made after Finney's method to restore the free passage of urine from the pelvis (fig. 3), but as it was found that the dilated pelvis did not drain well, nephrectomy was performed. The kidney substance was not found to be much destroyed. The patient made an excellent recovery.

*Case IV.*—Large left hydronephrosis (kidney substance mostly destroyed) due to abnormal renal artery grooving the ureter. Nephrectomy.

L. G., a patient under the care of Mr. J. Sherren, was subject to severe attacks of abdominal pain for twenty-five years—i.e., from the age of 19 to 45

—then the attacks entirely ceased. The attacks came on suddenly at any time, irrespective of exertion or movement; they lasted about twenty-four hours, "doubled her up," and made her vomit. No urinary symptoms were noticed, but the doctor who treated her discovered a tumour in the left side of the abdomen, which was fairly uniform. On admission to the London Hospital (at the age of 48) this tumour was readily seen and felt; it moved freely in all directions. A vertical lumbar incision revealed an enormously dilated pelvis with the remains of the kidney situated at its upper part. The ureter and renal vessels were ligatured and nephrectomy performed. An abnormal renal artery was found crossing the ureter, and causing a groove in it; below this point the ureter was contracted, above greatly dilated. The patient made an excellent recovery.

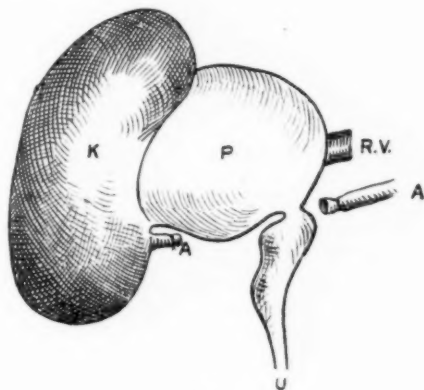


FIG. 4.

Extreme constriction where the aberrant artery, A, crossed the pelvis, P,  
(Case V.)

*Case V.*—Attacks of right-sided abdominal pain for a year. Excision of vermiform appendix (normal) followed by exposure of right kidney and division of aberrant renal artery which obstructed ureter.

W. H., aged 20, first suffered a year ago from attacks of pain in the right side of abdomen and loin. These attacks came on gradually, making him sick; local warmth relieved him. There were no urinary symptoms of any kind. Six months elapsed between the first and second attacks, but then they recurred every week. There were no abnormal physical signs and Mr. H. M. Rigby found nothing abnormal on cystoscopic examination. Skiagrams were also negative. The vermiform appendix was first examined through the usual incision in the right iliac fossa; it was normal and was removed. After closure of this wound in layers the patient was turned on to the left side and the right kidney exposed. The renal pelvis was found

dilated and tortuous owing to an aberrant "tail" artery (fig. 4). This was divided between two ligatures and the ureter straightened. The pelvis was seen to empty itself. The renal capsule was then incised and reflected; its two portions were secured by stitches traversing the lumbar muscles. Recovery uncomplicated.

*Case VI.*—Nephralgia of five years' duration. Exploratory lumbar incision, inferior renal artery found in front of the ureter, division of vessel between ligatures.

L. S., aged 36; admitted under Mr. Hugh Lett with a history of attacks of pain in the right loin since the age of 31. The pain was of a dull, aching character and was brought on by walking or a jolting movement; nothing relieved it, but she lay by preference on the affected side. There was occasional pain on micturition and the patient said the urine was thick and cloudy after an attack. There were no abdominal physical signs; the right kidney was not displaced. Mr. Lett explored the kidney through a lumbar incision, and found an abnormal artery going to the lower pole of the kidney which crossed in front of the ureter. This vessel was divided between ligatures and the kidney fixed in position by sutures. A fortnight after the operation there was some recurrence of pain with sickness.

*Case VII.*—Hydro- and pyo-nephrosis on right side due to obstruction of ureter by abnormal artery. Kidney disorganized. Nephrectomy.

G. A., at the age of 27, became the subject of paroxysmal attacks of right-sided abdominal pain which "doubled him up" and caused vomiting. The attacks came on chiefly in the morning and got worse during the course of the day. Nothing abnormal was to be felt in the abdomen. With the cystoscope the right ureteric orifice was seen to be congested with one or two hæmorrhages round it. A slight trace of albumin had been sometimes present in the urine. Mr. Russell Howard, under whose care the patient was, explored the right kidney from the loin, finding it white and cystic, with greatly distended pelvis containing purulent fluid. Nephrectomy was performed; the ureter was found to be obstructed 2 in. below the pelvis by an abnormal renal artery. The patient made a good recovery. On microscopical examination the epithelium of the pelvis was found to be intact and thickened. There was chronic interstitial inflammation with hæmorrhages in the remaining kidney tissue.

*Case VIII.*—Attacks of right lumbar pain, then eight years' interval; recurrence of pain. Operation, ureter found to be obstructed by abnormal artery, vessel divided between ligatures.

A. B., at the age of 38, became liable to attacks of right-sided abdominal pain; he attended as an out-patient for six weeks, and was then quite free for eight years, when the attacks recurred. The pain was always worse in the daytime and when walking; it caused vomiting and profuse sweating.

but no increased frequency of micturition or hæmaturia. The urine contained a trace of albumin and pus. The pain was unusual as these cases go, in that it radiated from the right kidney region into the groin and down the thigh to the knee, sometimes to the testicle. X-rays and the cystoscope showed nothing abnormal. Neither kidney could be felt. Mr. Milne explored the kidney through a lumbar incision. It was movable; an aberrant artery crossed the ureter to the lower renal pole about 1 in. below the pelvis. The artery was divided between ligatures; the kidney replaced without any special fixation being done. Rapid recovery.

*Case IX.*—Right hydronephrosis due to kinking and obstruction of ureter by an aberrant artery. Nephrectomy.

E. B., aged 33, was attacked sixteen months before with right-sided abdominal pain, coming on every fortnight or so and lasting twenty-four to

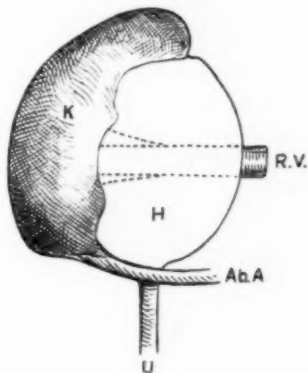


FIG. 5.

Abrerrant artery entering the extreme lower pole of the kidney. (Case IX.)

forty-eight hours. It made him vomit, but he noticed nothing abnormal as to frequency of micturition. The pain was felt all over right lumbar region and down to the buttock; it came on sometimes when lying down, and was somewhat eased by lying on the affected side. There was occasional slight hæmaturia. In University College Hospital a skiagram was made with negative result. He was admitted to the London Hospital under Mr. H. M. Rigby, who found by the cystoscope that the right ureteral orifice was "congested and about twice as long as the left one." At the operation the kidney was found to be adherent, not enlarged, but the cortex thinned out by greatly dilated pelvis and calices. An abnormal renal artery crossed in front of the lower part of the pelvis, constricting and kinking it (fig. 5). Nephrectomy was performed. Perfect recovery.

*Case X.*—Kinking of right ureter from pressure of abnormal vein coming from kidney. Operation.

R. L., aged 46, was admitted under Mr. E. H. Fenwick for (1) almost constant pain in right side of abdomen, radiating towards right testicle and occasionally making him sick; (2) very occasional hæmaturia. There was no abnormal frequency of micturition. In the absence of any indication of stone or tubercle Mr. Fenwick operated and divided the obstructing vein with good result, but further notes are wanting.

*Case XI.*—Kinking of right ureter below a high-placed pelvis by a posterior renal artery, which was divided. Fixation of kidney capsule to muscles.

J. T., from the age of 31, was liable every few days to attacks of sharp shooting pain in right side of abdomen (hypochondrium, &c.), sometimes coming on at night-time. Gall-stones were suspected. The pain radiated "towards the left arm" (?) and down towards the right groin and testicle. Skiagram negative; Urine normal. Mr. E. H. Fenwick found at the operation the pelvis of the right kidney placed abnormally high, 2 in. from the top there was an abnormal posterior renal artery which caused obstruction and was divided. The kidney capsule was divided and sutured to the muscles, the exposed surface of kidney being touched with pure carbolic acid. Some suppuration followed. Patient was well on discharge.

*Case XII.*—Hydronephrosis due to obstruction of right ureter by small aberrant renal artery and vein. Independent cystitis (?), leaving persistent slight pyuria.

W. M., a soldier, at the age of 14 was successfully treated in Brighton Hospital for tetanus with an antitoxin. Otherwise he was healthy until the age of 18, when after a severe chill he passed some blood and pus in the urine, and was said by his doctor to have cystitis. He was in hospital for five weeks and returned to work free from pain but with his urine still slightly thick. As soon as he started riding again the pain returned in the right loin, "as sharp as a knife," doubling him up, and making him sweat and occasionally vomit. The patient was admitted under the care of Mr. E. H. Fenwick, who found a generally congested bladder—"iridescent, such as is seen in some cases of renal calculus" (E. H. F.) Examination by X-rays and laboratory tests were negative as to stone or tubercle. Mr. Fenwick operated by the usual lumbar incision; the pelvis was felt to be enormously dilated, the kidney was very deeply placed and movable. The ureter was traced with some difficulty owing to the strength of the muscles, &c. No other stone was found, but the ureter was found to be kinked at its junction with the pelvis by a small aberrant artery (accompanied by its vein) which ran from the aorta to the lower pole (fig. 6). These vessels were divided between ligatures. Drainage and suture of wound. Patient left three weeks after the operation, apparently quite cured.



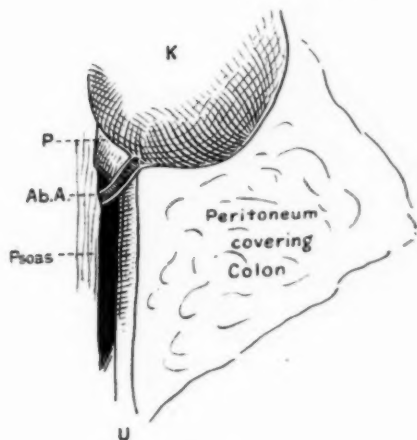


FIG. 6.

Small aberrant artery (**Ab. A.**) obstructing the ureter. **P**, pelvis of kidney (**K**).  
(Case XII.)

*Case XIII.*—Aberrant renal artery going to lower pole of left kidney behind the ureter and not obstructing it. Calculi in this kidney, removed by nephrolithotomy; section of abnormal artery.

**S. A.**, aged 18. Attacks of renal colic lasting about twenty-four hours, coming on once a week, brought on by sudden movement; pain radiating towards testicle. X-rays showed evidence of two stones in the kidney. At operation it was found impossible to lift the kidney into the wound owing to abnormal renal vessels which anchored the lower end of the kidney into which they ran. After ligature and division of these vessels the kidney was drawn towards the surface, its convexity incised, and two large, with several small, calculi were extracted. Renal wound sutured with catgut. Recovery uninterrupted. The abnormal artery was only 2 mm. in diameter; it ran behind the ureter, and "had caused no constriction at all." The kidney was lobulated. The patient was under the care of Mr. James Sherren.

In another case under Mr. E. Hurry Fenwick—a man, aged 32—whilst nephrolithotomy was being performed an aberrant renal artery was found to be entering the upper pole of the kidney. This was avoided by incising the kidney towards its lower end.

*Case XIV.*—Intermittent right hydronephrosis with severe attacks of pain due to ureter being kinked by undercurrent artery.

**A. B.**, a bricklayer, aged 28, was admitted under the care of Mr. E. Hurry Fenwick. At the age of 23 he became subject to attacks of right abdominal

pain occurring every two or three weeks, making him sick and doubling him up. He had been long under treatment by diet and medicines. He found the pain relieved by lying down, by local heat, by taking lithia and potash, and slightly by taking food. The attacks were brought on sometimes by taking exercise. At the end of four years (no doubt owing to the pelvis having stretched greatly) the pain became less severe and colicky in character and was a dull, monotonous ache. He described it as commencing 1 in. below the last rib outside the lumbar spines and spreading forwards on the same level to about 1 in. internal to the anterior superior spine. The urine was normal, there was no abnormal frequency. It may be noted that when a boy he had frequent "bilious attacks," which may have been renal pain, as the subsequent severe ones were also put down to "liver." On admission a uniform tumour was felt to descend with respiration below the right ribs; it is described as hard. At the operation, Mr. Fenwick found that the kidney lobulated, the pelvis distended. This was punctured and the urine drawn off. The ureter was then seen to be kinked over an aberrant artery, the bag of distended pelvis projecting downwards on inner side of the ureter. These two were anastomosed by sutures after cutting out a piece of each. The renal capsule was anchored without division to the muscles by catgut. Drainage of wound. For some three weeks urine escaped from the wound and there was some blood and pus found in the urine. He left the hospital four weeks after the operation. Three weeks later he was looking better and had gained weight. He still had dull pain in the back at times, but nothing like the old pain in severity.

*Case XV.*—Floating right kidney, ureter kinked by aberrant artery. Chief symptoms: Extreme frequency of micturition and dull, aching pain in the loin. Artery divided and ureter straightened, kidney capsule being fixed to the last rib.

G. H., aged 25, single; house-work. Was quite well until five months before admission. Was then suddenly taken with an attack of frequent micturition—thirty times in the day—without pain. Four days later the frequency occurred, this time with a good deal of pain in the middle of back, and recurred often. At the end of two or three months the pain settled in the right loin; it did not radiate; there was never either hæmaturia or colic. She became much troubled with headache, and lost weight (1 st.). She was admitted under the care of Mr. James Sherren. Neither X-rays nor the cystoscope revealed abnormality. The urine contained oxalate of lime crystals but no blood. The kidney was somewhat floating, the lower pole tilting forwards. At the operation, which was rendered difficult by the small space between ribs and iliac crest, Mr. Sherren found an aberrant renal artery entering the lower pole, on which the ureter was kinked and narrowed. This artery was clamped and ligatured, the ureter straightened out, the renal capsule reflected and sutured to the last rib. The amount of urine passed each day before the operation was less than normal, and it continued to be so during her stay in

hospital—i.e., about 20 or 40 oz. The frequency was, for the fortnight subsequent to the operation, ten times or more in the twenty-four hours, but gradually diminished to about eight.

*Case XVI.*—Right hydronephrosis of large size, disappearing at times; lumbar pain but no abnormal frequency or other urinary signs. At operation a large aberrant artery was found in front of and kinking the ureter.

W. D., aged 27, a clerk, came under the care of Mr. H. M. Rigby with the history of right-sided pain and slight tenderness in the loin. A very obvious lump was felt pushing forward the right rectus muscle and reaching as low as the umbilicus. There were no urinary symptoms, and the X-rays showed nothing abnormal. The lump was found to vary from time to time and was diagnosed as a hydronephrosis. The kidney was felt to be somewhat floating. At the operation Mr. Rigby found a greatly dilated pelvis, the ureter was bent over and obstructed by a large aberrant artery which entered the lower pole, running in front of the ureter. The artery was tightly stretched. It was ligatured and divided. Perfect recovery.

*Case XVII.*—Movable left kidney with dilatation of pelvis due to kinking of ureter over abnormal artery. Division of vessel and fixation of kidney. Repeated recurrence of attacks of pain after the operation with hæmaturia on one occasion. Subsequent recovery.

H. R., a chauffeur, aged 21, under the care of Mr. E. H. Fenwick. Unfortunately the notes as to character of the pain, &c., are wanting. The case is, however, worth including, because of the recurrence of lumbar pain three weeks after the operation when the patient got up for the first time, when the wound was soundly healed. Several times colicky pain recurred with vomiting, and on one occasion hæmaturia.

*Case XVIII.*—Attacks of left lumbar pain for five years; no urinary symptoms; nephrorrhaphy performed without relief; at subsequent operation aberrant artery found to obstruct ureter. Division of the vessel; cure.

A. B., from the age of 16 was subject to attacks of dull, aching pain, always on the left side, independent of exercise, and occurring sometimes when she was in bed, coming on every few days. At the age of 20 she was admitted under the care of Mr. E. H. Fenwick and nephrorrhaphy was performed. She kept well for three weeks and then the attacks of pain recurred, unattended with any urinary symptoms. She was a thin subject and both kidneys could be felt: the left one was plainly well fixed in position. Mr. Fenwick explored the kidney again and found the pelvis dilated, the ureter bent and obstructed over a "tail" artery running behind it, which was ligatured and divided. Fresh catgut sutures were used to secure the kidney again in position. For a week the patient had considerable pain, but made an excellent recovery and left the hospital quite well.

*Case XIX.*—Intermittent left hydronephrosis due to a large aberrant artery (the size of the brachial) running behind the ureter to the lower pole of the kidney. Artery divided; part of dilated pelvis excised.

F. B., from the age of 17 became subject to attacks of very severe pain in the left lumbar region; these attacks came on only in the daytime and continued intermittently for nine years. The pain was so severe that she would be "doubled up," and roll on the floor in agony, sweating profusely and vomiting. As usual the sickness relieved the pain, but contrary to the general rule she could not bear the least pressure on the affected side and had to undo her clothes to get a little relief. She was pregnant twice, and during pregnancy was free from the attacks. After being liable to them for nineteen years, and as they became more frequent and severe, she came under the care of Mr. Hurry Fenwick. The abdomen was flaccid and the left kidney could easily be felt; it appeared to be nodular. There were no urinary symptoms, nor had there ever been (except perhaps diminution in quantity). The X-rays showed nothing abnormal. The kidney was not floating; at the operation it was found to be fixed in position. Mr. Fenwick found exposure of the kidney to be very difficult owing to the costo-iliac space being narrow and the patient's muscles thick; it was impossible to draw the kidney into the wound. A firm, rounded lump was felt at the lower and posterior aspect of the kidney; this was incised and urine escaped, the cystic lump being obviously the distended pelvis. The cause of this being sought, no stone could be found; the ureter was exposed low down in the wound with much difficulty and traced upwards. It was found to be kinked over an abnormal renal artery of large size (brachial), running across from the aorta behind the ureter to the tail of the kidney. This artery was tied in two places and cut across, thus relieving the ureter. Part of the dilated pelvis was cut away and the edges sewn together. Drainage. (The notes of this most interesting case were written by Mr. F. S. Kidd.) Some mild suppuration followed, but the patient left the hospital five weeks later, quite relieved of pain and in good health.

*Case XX.*—Very localized attacks of left lumbar pain due to kinking of ureter by aberrant "tail" artery. Division of the vessel.

E. F., married, at the age of 22, had a sharp attack of pain in the left loin; this was early in a pregnancy. For eight months or so she was free from pain, and it was only four months after the child was born that the second attack came on, to be followed by many others. The pain caused sickness, was relieved by heat applied locally and by the half-sitting posture. Local pressure during an attack increased the pain. She was admitted (one year after the commencement of symptoms) under Mr. H. M. Rigby. There were no urinary symptoms of any kind (a little pus was present in the urine, but this is so frequent in women as to be of no account). The X-rays showed nothing abnormal, nor did the cystoscope. Lumbar exploration showed an aberrant artery coming from the aorta across the pelvis to the extreme lower

pole of the kidney, passing in front of and kinking the ureter. "The inflammation and adhesion round the lower pole must have increased the pressure of the vessel recently" (note by Mr. F. S. Kidd). The abnormal artery was divided between ligatures, and the wound closed in layers without drainage. Six days later it was necessary to give an anæsthetic and insert a drainage-tube owing to rise of temperature and repeated vomiting. A little pus was let out. Good recovery, but the urine continued always to show some pus in it.

*Case XXI.*—Attacks of right abdominal pain for eight years; hæmaturia; right kidney somewhat floating (?). Hydronephrosis found due to aberrant artery.

R. A., at the age of 22 had a sudden attack of pain in the right lumbar region and iliac fossa; this lasted a week. Twelve months later another severe attack came on (there were slight ones in between these). Appendicitis was diagnosed. Then for four years she was quite free; then, after passing "black urine," she was seized with severe pain again. The hæmaturia lasted for a day, and recurred with repeated attacks of the pain. She was a nurse working in India and other countries abroad, and her case was investigated by many surgeons—sarcoma of the kidney being suggested, and (after examination under anæsthetic) floating kidney. She came back to England and was in St. Bartholomew's Hospital, where no conclusion was arrived at. The pain was worse on taking exercise, and was relieved by lying down, especially on the right side. During the daytime there was frequent micturition, but only once in the night. When admitted to the London Hospital under Mr. E. H. Fenwick there had been no hæmaturia for some months, but as she was a nurse by profession it can hardly be doubted that her observation of previous bleeding was correct. She was aged 30, was married, and had two children. During the pregnancies she had slight blood-spitting. The urine contained some pus; otherwise there were no abnormal signs, cystoscopic and X-ray examination being negative. Mr. Fenwick operated by lumbar incision. "The kidney showed marks of previous mobility, and there were many soft parts in the cortex, indicating backward pressure. The pelvis was dilated. The ureter was isolated and found to be kinked over an artery running to the lower pole." This was cut between ligatures; the pelvis emptied itself. A rectangular flap of capsule was then reflected from the middle of posterior aspect of the kidney and sutured to the arcuate ligament. Excellent recovery.

*Case XXII.*—Right-sided hydronephrosis due to obstruction of the ureter by an aberrant artery crossing it in front; carcinoma (hypernephroma) of the same kidney. Nephrectomy.

This case, the notes of which Mr. H. M. Rigby very kindly placed at my disposal, is the only example I have come across of the coincidence of obstructed ureter and new growth of the kidney. It is, moreover, of special interest from another point of view. Although the renal pelvis had become

much distended, the only history of recurrent attacks of pain referred to two occasions—one seven years and the other seven months before operation—at the ages of 50 and 57 respectively.

A. B., aged 58. In 1904 patient had an attack of (?) appendicitis. He was laid up for four to five months; no jaundice. In May, 1905, patient had a growth removed from the lip; this was not examined by microscope. He has had no serious illness since then until last September (1910), when he was in Lowestoft. He then had severe pain in the abdomen, sickness and diarrhoea. He was in bed for a fortnight. Three months ago his doctor accidentally noticed a tumour in the region of the liver. Patient has had no symptoms at present. It has been noticed that he is thinner. Examination (April 19, 1911): There is a large, lobulated tumour on the right side, evidently in connexion with the right kidney; freely movable; it has the colon in front of it and is separated from the liver edge. It is lobulated on the surface, but smooth; does not feel like a fluid swelling. Examination of urine: Cloud of albumin; specific gravity, 1016; acid; no obvious deposit. No crystals or abnormal epithelium were seen. The patient was under the care of Mr. H. M. Rigby in private, and the diagnosis of hydronephrosis, with perhaps a solid renal growth as well, was made.

Operation (May 22, 1911): An exploratory incision was made in the right loin and the tumour of the kidney freed and displaced from the surface. It was found to be a large cystic kidney with a tumour attached to the lower and posterior part of the convex surface. The pelvis was much distended. The ureter was caught up and "strapped" by a vessel passing in front and below, an acute kink being formed at the juncture of the ureter and pelvis. The vessels of the kidney were ligatured separately, silk for the artery, chromic gut for the vein, and chromic gut for the ureter. On examination the tumour at the lower pole was found to be a large growth, which, on section, appeared to be of the nature of a hypernephroma. The loin muscles were sutured with chromic gut and a drainage-tube fixed in position. The patient made an excellent recovery.

The following is the microscopical report of the tumour made in the London Hospital Pathological Department: Tubular and papillary, cylindrical and short columnar-celled carcinoma of kidney (Grawitz's tumour). The growth consists of masses of close-set tubules and long branching papillary processes. These processes have a very delicate stroma of spindle cells with occasional small blood-vessels. They are covered by a layer of short columnar cells, the nuclei of which are at different levels, so that occasionally there appear to be several layers of cells. In part these cells are degenerate, having a swollen, finely granular or vacuolar protoplasm and a compressed eccentric nucleus. There is hæmorrhage in parts. The fibrous capsule varies in thickness; it appears to be invaded by the growth.

It is best to regard the co-existence of renal tumour and obstruction of the ureter as purely accidental and not in the nature of cause and effect. What-

ever view is adopted of the origin of hypernephroma (Grawitz's tumour), there is practically no evidence at all that its development is favoured by obstruction to the urinary flow. With regard to the diagnosis, it should be noted that hæmaturia was absent in this case, and that the renal swelling was noticed almost by accident. Were the two attacks of abdominal pain, for which he laid up, caused by the vascular obstruction of the ureter? The first one may safely be disregarded, and about the second attack we must be in doubt, as it was accompanied by diarrhœa—a very unusual and unexplained complication of obstruction to a ureter. We may conclude that in this case either no subjective symptoms were caused by this obstruction or only one solitary attack of pain (at the age of 57).

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## DISCUSSION.

Mr. FRANK KIDD said he had recently purchased an old anatomy book of the seventeenth century written by Nicolas Culpepper, and in one of the diagrams there was pictured an abnormal artery running behind the ureter to the kidney. That showed how accurately some of the old anatomists observed and figured what they found. He thought that the Fellows might be interested to know that the coloured photographic print of a kidney shown by Mr. Hutchinson, and which had evidently caused surprise from its excellence, had been taken from the fresh specimen by his brother, Mr. Dudley Kidd. The result was a colour-print on paper in natural colours, far more accurate than any other method of figuring a specimen, such as a water-colour drawing. He did not think it was at all widely realized what perfect results could now be obtained by an expert in colour photography with prints on paper. The value of such accurate reproductions was obvious. Mr. Hutchinson said he had collected all the cases from the London Hospital records, but he seemed to have omitted two cases which had been under Mr. Kidd's care, one of which was of interest as the man's symptoms had been profuse hæmaturia lasting for months, and which had been completely relieved by operation. There was now a method available by which it was possible to diagnose "dilated renal pelvis." As one of the commonest causes of dilated renal pelvis was an abnormal artery, a shrewd guess could usually be made that such a condition was present. The method consists in passing a ureteric catheter without any anæsthetic and filling the pelvis of the kidney with collargol, after which a skiagram is taken and brings out the size and shape of the kidney, the calices and the pelvis, and how many kidneys and ureters are present (such a specimen was exhibited on the screen). According to the Mayos' latest figures one out of every twenty-five kidney operations had to do with a congenital abnormality. This was only another illustration of the fact that nowadays a man ought to be a master in the art of passing a ureteric catheter before undertaking kidney surgery.

Mr. ALFRED JOHNSON said that the importance of aberrant renal vessels had not, he believed, been realized in the past. By some authorities the proportion of cases in which accessory arteries were found was placed as high as 14 per cent. That was the proportion given for abnormal arteries, and abnormal veins were said to be even commoner. These vessels might be important during any operation on the kidney, and a knowledge of their occurrence might prevent unnecessary hæmorrhage. Their greatest interest, however, arose from their relationship to distension of the renal pelvis. In 1909 Mayo stated that there were aberrant vessels in twenty out of twenty-seven cases of hydronephrosis on which he operated, and in thirteen of those the division of the aberrant vessel led to relief of the condition. He agreed with Mr. Kidd that one result of recent work on the examination of

the kidney should be to lead to early diagnosis of distension of the renal pelvis, which, according to Mr. Hurry Fenwick, was the commonest cause of renal pain. He (the speaker) thought that the most trustworthy method of showing this distension was by pyelography. It had been suggested that the capacity of the renal pelvis might be measured by catheterizing the ureter and noting the quantity of urine which came away in a steady flow. He did not think that was a reliable method. Another proposal was to inject the renal pelvis with saline or other fluid and measure the amount which could be introduced. This method was likely to give a misleading idea of the size of the renal pelvis, for some of the fluid injected might find its way down the ureter outside the ureteral catheter. This source of error was shown by the fact that, on injecting the pelvis with collargol for pyelography, he had recovered collargol from the bladder before the catheter was withdrawn from the ureter. The best method of ascertaining the size of the renal pelvis was to fill it through a ureteral catheter with some material such as a solution of collargol, which was opaque to the X-rays, and then skiagraph the kidney. If the dilatation of the renal pelvis was found to be great, or if, after repeated examination, a slight dilatation was seen to be increasing, operative treatment should be undertaken. If dilatation of the renal pelvis was demonstrated and there was no abnormal mobility of the kidney, no evidence of stone or of any other cause of obstruction to the flow of urine along the urinary tract, it might well be that the distension was due to an aberrant renal vessel and an operation for the relief of the condition might be undertaken deliberately. Mr. Johnson mentioned a case which had come under his care in which a diagnosis of gall-stones or appendicitis had been made by a medical man. Cystoscopy revealed an elongated, turgid, dilated orifice of the right ureter, and pyelography showed a marked dilatation of the renal pelvis. The skiagram was shown on the epidiascope with a skiagram of a normal renal pelvis of the same type for comparison. In this case no cause for the dilatation of the pelvis had been found as yet and it might well prove, on operation, to be due to an aberrant renal vessel.

Mr. McADAM ECCLES said he recently had had a case bearing on the subject of the paper in a middle-aged woman, who fifteen months ago had signs of intermittent hydronephrosis. It was thought possibly to be due to mobility of the kidney. The kidney was mobile, but not to such an extent as to render kinking of the ureter very likely. The kidney was cut down upon from the loin by a colleague and was sutured, but she continued to have the intermittent hydronephrosis. He saw her a year afterwards, and then the kidney seemed to be quite fixed in the loin as the result of the operation. When he saw her she had one of the attacks, and the kidney was projecting forward so much that the lower pole of it appeared almost like a pyramid underneath a very thin abdominal wall. He had never seen a hydronephrosis quite of the same character. He considered it was probably

due to an aberrant vessel. He therefore made an anterior incision through the right linea semilunaris, and could demonstrate to everyone in the operating theatre a vein coming across the lower part of the pelvis of the kidney; the dilatation was almost entirely confined to the lower third of the organ. It was this portion which had been projecting forwards. As he divided the vessel between the two ligaments, the dilated portion collapsed, thus demonstrating the cause which bore so definitely upon the present discussion.

Mr. ARTHUR BARKER remarked that Mr. Johnson said that together with the dilatation of the pelvis of the kidney on that side there was a dilatation of the ureter at its bladder orifice. He did not know whether that was usual, but it was interesting to hear that it might be so. He was in a difficulty—namely, that if the ureter were dilated the whole way up why should there be an obstruction to the flow of the urine?

Mr. JOHNSON, in reply to Mr. Barker, said that there was some elongation and dilatation of the orifice of the ureter in the case which he had mentioned and that had been recognized for some time as a sign of dilatation of the pelvis of the kidney. Mr. Hurry Fenwick had pointed out that marked elongation of the ureteric orifice, the lips being turgid and swollen, was almost a diagnostic sign of dilatation of the renal pelvis.

Mr. HUTCHINSON, in reply, said he knew of the method of distending the pelvis with collargol and had seen photographs, but it was too recent a matter for any of his cases to have been examined by that means. It obviously would enable one to detect cases of dilatation of the pelvis earlier than would have otherwise been possible. But it was also equally obvious that it would not enable one to tell when the dilatation was due to an aberrant artery. The photograph shown was not a case of aberrant artery definitely, though it might have been. He did not mention Mr. Kidd's cases, as he hoped he would be present to join in the discussion and refer to his own cases. He was especially interested to hear Mr. McAdam Eccles's description of his case which was on all fours with two which he (Mr. Hutchinson) mentioned, where the kidney in each case was supposed to be floating and was stitched by a well-known surgeon, and the aberrant vessel missed. Its presence was only revealed by a second operation. That showed that the subject was not yet sufficiently in the minds of surgeons, and for that reason he brought the communication before the Section.

## Case of "Banti's Disease" cured by Splenectomy.

By FRANK KIDD, F.R.C.S.

L. L., AGED 17, a shop assistant, was first admitted to the London Hospital on December 15, 1910. She had been sent by a doctor on October 13, 1910, to Barking Fever Hospital as a case of typhoid fever, she having been ill for one week with fever (temperature 103° F.), diarrhoea, and enlarged spleen. The doctor at the fever hospital found that there were no true signs of typhoid fever, and the Widal reaction proving negative she was sent home, the fever having also abated.

On November 3 she was again prostrated with a bout of fever which lasted about ten days, and then left her for about ten days. She continued to have these bouts with periods of remission until December 15, 1910. On that day her abdomen suddenly began to swell almost visibly, and she was brought up in a hurry by a nurse to the London Hospital. The nurse declared that the abdomen was twice the size when the patient got out of the cab as when she got into it.

On examination the abdomen was found to be shiny and distended with ascitic fluid. There was no fever, no anæmia or pigmentation of the skin, no œdema of legs, no enlarged glands; 208 oz. of clear fluid were obtained by tapping, and it was then clear that the spleen was enormously enlarged; but that the liver was not to be felt enlarged. The heart and lungs were clear, and the urine normal. The fluid contained mononuclear cells only and was sterile, nor could any tubercle bacilli be found therein. There was no history of syphilis, congenital or acquired, and no family history of splenic anæmia. The Widal, von Pirquet, and Wassermann reactions were all negative. Blood counts (*see chart*): Erythrocytes, 4,100,000; hæmoglobin, 85 per cent.; colour index, 1; leucocytes, 1,700; polynuclear neutrophiles, 46 per cent.; small lymphocytes, 32 per cent.; large lymphocytes, 13 per cent.; large hyaline, 9 per cent. Weight: 5 st. 11 lb., December, 1910; 6 st. 4 lb., January, 1911.

Progress: There was no further ascites and no more fever, so that at the end of January, 1911, the patient was sent home feeling quite well. In January, 1912, an attack of severe hæmatemesis occurred which lasted one day, and left the patient so weak that she had to keep her bed for one month. In April, 1913, another attack of hæmatemesis

came on more severe than the former, and was accompanied by pain in the pit of the stomach. This left her very prostrate. In May, 1912, the patient noticed a lump in the abdomen which felt heavy but caused no actual pain, and again entered the London Hospital under the care of Sir Bertrand Dawson, who referred her to me for operation as a case of Banti's disease.

Physical examination: Well-marked anæmia and wasting; slight œdema of legs; skin a peculiar dirty yellow colour; no true jaundice. Temperature subnormal (97° F.); pulse-rate normal. Heart slightly dilated—hæmic bruit over pulmonary area; lungs and nervous system normal; spleen much enlarged; liver not felt; moderate ascites; no abdominal tenderness. Urine acid, specific gravity 1030, no bile, no albumin, no sugar, no deposit. Moderate polyuria to as much as 70 oz. in the twenty-four hours. No enlargement of lymphatic glands. Wassermann reaction negative. Blood count (July 18, 1912): Erythrocytes, 4,900,000; hæmoglobin, 75 per cent.; colour index, 0.75; leucocytes, 3,000 per cubic millimetre (*see chart*).

Clinical diagnosis: "Banti's disease," *third stage*, all Banti's crucial signs being present—viz., (1) splenic enlargement; (2) absence of enlarged lymphatic glands; (3) a moderate secondary anæmia; (4) leukopenia; (5) a course of some years; (6) periodic gastric hæmorrhages; (7) ascites, shrunken liver, clay-coloured skin; (8) absence of alcoholic or syphilitic history.

Operation (August 6, 1912): Anæsthetic, A.C.E. mixture. The skin was painted with iodine (2 per cent. in rectified spirit). An incision 5 in. long was carried through the outer portion of the left rectus abdominis muscle. A fair amount of clear ascitic fluid escaped. The liver was found to be hard, knobby, cirrhotic and shrunken under the right costal margin ("island" cirrhosis). The stomach and gall-bladder were normal. The spleen, which was very large, was adherent to the diaphragm by loose adhesions which contained immense veins with walls of extreme tenuity, and which tore and bled furiously at the slightest touch. These were divided between ligatures, great patience and care being required to prevent tearing and severe hæmorrhage. To save time when all adhesions had been freed, large flat sponges were pressed into the splenic bed, which controlled the remaining hæmorrhage for the time being. The spleen was now dislocated on to the surface and turned over on to the left side of the chest, and hereby the pedicle was exposed as a single broad sheet of peritoneum containing blood-vessels of great size. The vessels were

isolated by blunt dissection with the gloved finger and tied in series with interrupted silk ligatures from below upwards. The pedicle was then cut across and the spleen removed. The sponges were removed from the splenic bed, which was then surveyed, and several badly bleeding veins had to be caught up in artery forceps  $7\frac{1}{2}$  in. long. So deep were these veins that the handles of the forceps were below the surface of the wound. Great gentleness was required to prevent the forceps tearing off, fine silk ligatures having to be persuaded by the sense of touch alone over the tips of the forceps and tied. When this had been successfully accomplished and the hæmorrhage stanchied, a stab wound was made in the left loin for a drainage-tube, as it was clear there would be considerable oozing. The peritoneum was stitched with fine chromic gut, the muscles with stout chromic gut, and the skin with silkworm gut. Dry gauze dressings and copious splintings of cotton-wool were applied and the abdomen firmly bandaged. There was very little shock and convalescence was rapid. The wound healed by first intention and the patient left the hospital four and a half weeks after operation, having put on flesh and attained a healthy colour.

The blood counts appended show that the erythrocytes *at once* increased in number and improved in hæmoglobin content. The number of leucocytes increased, chiefly the polynuclear neutrophile and the large hyaline. This would probably be the effect of the absorption of blood-clot and the healing of the wound.

The patient was seen on October 21, 1912, by Sir Bertrand Dawson. Note: Good colour. Feeling in excellent health. Weight, 8 st. 1 lb., 9 oz. The abdomen showed no ascites. Liver barely felt. No tenderness. Abdominal wall rather flabby and unduly fat. The blood examination showed that the erythrocytes had increased by nearly 2,000,000 per cubic millimetre of blood. The hæmoglobin was 92 per cent. and the leucocytes had increased by 2,000, the increase being due to the large lymphocytes.

The patient was again examined on May 1, 1913. The weight was 8 st. 5 lb. The skin was a natural colour and there was no anæmia. The palpable lymphatic glands were not enlarged. There was no trace of ascites nor of œdema of the legs. The abdomen was flat and firm. The liver could not be felt. The scar was perfectly sound and hardly noticeable. The periods, which had ceased entirely for twelve months before the operation, have reappeared. Blood count: Erythrocytes, 5,900,000 per cubic millimetre; hæmoglobin, 90 per cent.; colour index, 0·8; leucocytes, 5,000 per cubic millimetre; polynuclear



neutrophiles, 45.5 per cent.; polynuclear eosinophiles, 8.0 per cent.; small lymphocytes, 17.0 per cent.; large lymphocytes, 27.5 per cent.; large hyaline, 6.5 per cent.; coarsely granular basophiles, 0.5 per cent.

PATHOLOGICAL REPORT, BY H. M. TURNBULL, M.D., AND  
G. B. BARTLETT.

*Chronic Inflammation of Spleen.*—The trabeculae are distinct but not thicker than normal; there is a marked congestion and dilatation of the veins in the trabeculae and there is hæmorrhage in and around most of the trabeculae. Malpighian bodies are few in number and are not large. Some of them show well-marked "germ centres." The spleen pulp, especially in the neighbourhood of the hæmorrhage, shows an increase in the collagen fibrils of the reticulum with some increase of the oval nucleated reticulum cells. The blood spaces are consequently smaller than normal. There are a good many neutrophile polymorphs with some lymphocytes and an occasional eosinophile cell in the blood spaces. The changes in the spleen are similar to those found in splenic enlargement with cirrhosis of the liver.

The terms "Banti's disease" and "splenic anæmia," have till now been used as convenient clinical shorthand expressions to cover a certain type of case that can be recognized clinically, and that can be cured or at any rate relieved of symptoms for a long time by splenectomy. Banti was the first to describe the clinical aspect of these cases in the following papers: (1) "Dell' anemia splenica," *Archivio della Scuola d'Anat. Patologica*, Florence, 1883, ii, pp. 53-122; (2) *La Semaine Médicale*, 1894, p. 318. He stated that the microscopical changes in the spleen were specific, a statement with which many pathologists do not agree. He referred to operations by Spencer Wells and others to show that cure was possible by splenectomy. In *Folia Hæmatologica*, 1910, x, p. 33, (quoted by Moynihan), he has collected fifty such cases where splenectomy has been performed. Cases operated on in the first stage, four cases with two recoveries; in the second stage, twenty-two with thirteen recoveries; and in the third stage, four with one recovery. Cases operated on in the third stage (to which my own case belongs) with a successful result are therefore very uncommon.

The hypothetical explanation brought forward by Banti in 1894 is the conception of some hypothetical poison settling in the spleen, leading to cirrhosis of the spleen with consequent anæmia and thence to intoxication and cirrhosis of the liver.



BLOOD EXAMINATIONS MADE BY DR. P. N. PANTON, DR. H. L. TIDY, AND DR. J. MANACK.

| Date ..                        | December, 1910 | July 18, 1912 | July 31   | OPERATION |          | August 8                        | August 9                        | August 10 | August 12                        | August 13 | August 20                        | August 22                       | May, 1913 |
|--------------------------------|----------------|---------------|-----------|-----------|----------|---------------------------------|---------------------------------|-----------|----------------------------------|-----------|----------------------------------|---------------------------------|-----------|
|                                |                |               |           | August 6  | August 7 |                                 |                                 |           |                                  |           |                                  |                                 |           |
| Erythrocytes ...               | 4,100,000      | 4,900,000     | 5,400,000 | —         | —        | 5,950,000                       | 5,550,000                       | 5,150,000 | 5,600,000                        | 5,500,000 | 5,400,000                        | 6,450,000                       | 5,900,000 |
| Hæmoglobin per cent.           | 85.0           | 75.0          | 75.0      | 80.0      | —        | 90.0                            | 90.0                            | 90.0      | 90.0                             | 90.0      | 85.0                             | 92.0                            | 90.0      |
| Colour index ...               | 1.0            | 0.75          | 0.75      | —         | —        | 0.8                             | 0.8                             | 0.8       | 0.8                              | 0.8       | 0.8                              | 0.7                             | 0.8       |
| Fresh blood ...                | —              | —             | —         | —         | —        | Rouleaux formation normal 5,000 | Rouleaux formation normal 5,000 | —         | Rouleaux formation normal 17,400 | —         | Rouleaux formation normal 11,720 | Rouleaux formation normal 5,000 | —         |
| Leucocytes ...                 | 1,700          | 3,000         | 2,800     | 6,600     | 7,800    | 5,000                           | 5,000                           | 11,300    | 17,400                           | 9,450     | 11,720                           | 5,000                           | 5,000     |
| Stained blood :—               |                |               |           |           |          |                                 |                                 |           |                                  |           |                                  |                                 |           |
| Polymorphonuclear neutrophils  | 46.0           | 53.5          | 59.5      | 62.0      | 84.5     | 70.0                            | 65.0                            | 70.0      | 64.0                             | 62.5      | 68.5                             | 41.8                            | 45.5      |
| Polymorphonuclear eosinophiles | —              | 0.5           | 0.5       | 1.0       | 0.5      | 0.5                             | 2.0                             | 3.0       | 0.5                              | 1.5       | 3.0                              | 6.0                             | 3.0       |
| Small lymphocytes              | 32.0           | 29.5          | 33.5      | 26.0      | 35.0     | 35.0                            | 10.0                            | 4.5       | 10.5                             | 10.0      | 11.5                             | 11.4                            | 17.0      |
| Large lymphocytes              | 13.0           | 8.0           | 3.0       | 5.5       | 4.5      | 2.0                             | 5.0                             | 1.5       | 3.5                              | 1.0       | 3.5                              | 40.6                            | 27.5      |
| Large hyaline cells            | 9.0            | 8.5           | 3.5       | 4.0       | 6.75     | 23.0                            | 22.0                            | 20.0      | 20.0                             | 23.0      | 12.5                             | 5.2                             | 6.5       |

Sutherland and Burghard,<sup>1</sup> in bringing forward two cases of splenectomy in children, do not accept this explanation, and hypothecate a functional loss of vasomotor control in the splenic artery which leads to over-activity of the spleen (just as Graves's disease is due to a functional over-activity of the thyroid gland). They accept the hypothesis that the spleen is the main "blood destructor" of the body, so that when its functional activity is increased there is an increased production of harmful katabolic blood substances. Hence arises the anæmia, the pigmentation of the skin, and the cirrhosis of the liver, and hence the immediate improvement and rapid cure when the spleen is excised.

Dr. H. M. Turnbull, the Director of the Pathological Institute at the London Hospital, has very kindly furnished me with the following information and has permitted me to bring it forward. Only four cases that could possibly be labelled as "Banti's Disease" or "Splenic Anæmia" have come to autopsy at the London Hospital in the years 1907-12:—

(1) Post-mortem 169, 1907. Male, aged 18. Admitted for hæmatemesis which proved fatal. Spleen 2 lb. 5 oz. Liver shows a peculiar form of "island" cirrhosis, that is to say, the fibrous strands are dense but few and far between and surround huge islands of regenerating liver cells. (Case fully described in *Pathological Archives of the London Hospital*).

(2) Post-mortem 67, 1909. Male, aged 25. Four years' history of anæmia, attacks of jaundice, hæmatemesis, huge spleen. Shown repeatedly as a case of Banti's disease. Death from hæmatemesis. Stones in gall-bladder, extra- and intra-hepatic ducts. Portal vein a fibrous cord. Spleen 2 lb. 1 oz. Liver very slight biliary cirrhosis.

(Note: This case should not have been diagnosed as "Banti." Jaundice does not occur in Banti. The discoloration of the skin is a peculiar form of pigmentation.)

(3) Post-mortem 1,094, 1900. Female, aged 6. Three years' history of anæmia, hæmatemesis, ascites. Death from peritonitis the result of tapping. No cirrhosis of liver. Varicose œsophageal veins. Spleen 15 oz. No obstruction could be found in portal venous system.

(4) Post-mortem 120, 1912. Female, aged 12. Hæmatemesis since the age of 18 months, eventually fatal. Rupture of dilated vein in mucosa of stomach. Extreme dilatation of lower œsophageal veins. No obstruction to splenic or portal vein found after careful search. Spleen 9½ oz. Liver not cirrhotic.

<sup>1</sup> *Lancet*, 1910, ii, p. 1819.

The impression left on the mind by this information is that it is very doubtful if "Banti's disease" is due to a single specific cause, but it is more likely a symptom-complex that may arise in any case where there is engorgement of the splenic veins. This engorgement might be active arterial hyperæmia, or a passive venous congestion from blockage of the splenic or hepatic veins by clot, by certain forms of cirrhosis of the liver ("island cirrhosis") peculiar to young people and not due to alcohol or syphilis, or by causes not determined.

An engorgement of the œsophageal veins in Cases 3 and 4 was the most noticeable feature of the autopsy, yet nothing could be found to account for it after the most careful search.

The most reasonable way to attempt to explain the extraordinary amelioration produced by splenectomy seems to be that of Sutherland and Burghard—namely, that an engorged and enlarged spleen causes increased blood destruction and a toxæmia that eventually proves fatal. It is possible that the removal of the spleen does not cure permanently, as the longest interval after operation is eleven years of apparent cure in Banti's first case, and I know of a case where the symptoms have returned and have proved fatal two years after an apparently successful operation. Still the fact remains that in the case I have brought forward to-night I was dealing with a woman who had been going downhill for four years, and in whom the operation revealed advanced cirrhosis of the liver and ascites; yet who after removal of the spleen has lost her anæmia, lost her ascites, lost her tendency to hæmatemesis, who has put on 3 st. in weight, and who thinks she has never been better in her life. Surely if such a result can be obtained this operation is fully justified.

The logical conclusion to my mind is that *splenectomy ought to be tried in all cases of cirrhosis of the liver with enlargement of the spleen*. It is possible that it is the enlarged spleen which is harmful to the body in such cases, and it is possible that splenectomy might cause amelioration for many years.

No one can give an answer to such a statement without putting it to the test of experience. I appeal to the physician to consider whether he might not recommend a trial of splenectomy in cases of alcoholic cirrhosis of the liver with enlarged spleen. It is possible the results might be quite as favourable as in these cases of cirrhosis of the liver in young people with enlarged spleens. Cases that at present are labelled Banti's disease are recommended with little hesitation for operation. It is very hard to see where the difference lies, except that in one case

the poison at work is known, in the other it is unknown, and that in one case the disease is supposed to be primary in the spleen, whereas it is quite conceivable that both may be primary in the liver.

And as regards the risks of the operation, it should not prove any more dangerous than omentopexy, which is frequently recommended and performed, and with results that are not so encouraging as to prohibit the trial of fresh methods of cure.

As regards the technique of the operation, the high mortality in some of the earlier cases was due to the failure to realize that there may be adventitious adhesions to deal with, and that these may contain enormously dilated thin-walled veins. Hæmorrhage can only be controlled by adequate exposure. A vertical incision near the outer border of the left rectus abdominis muscle 4 to 5 in. long is sufficient to start with and may suffice for the whole operation if there are no adhesions. But if adhesions are met with which tear and bleed easily the incision should at once be enlarged by a transverse cut from the outer edge of the wound outwards into the loin for an inch or more, as much as seems necessary. Such an incision gives a greatly increased exposure of the deeper parts of the wound and may prove life-saving if hæmorrhage is severe. It heals up soundly, and I have never seen a hernia follow such an incision in the cases in which I have employed it, cases chiefly of large renal tumour.

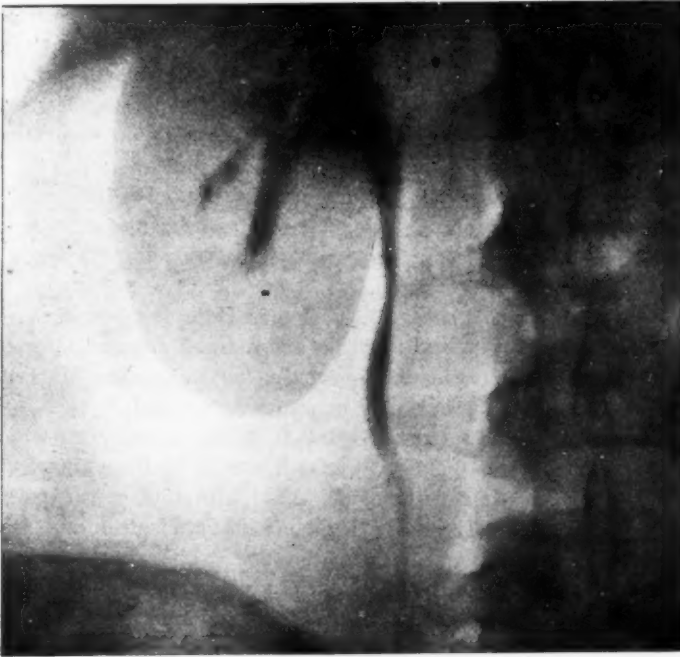
### **Case of Hypertrophy of Spleen ; Mobility, Rotation, Peritonitis, Adhesions ; Operation for Removal of Painful Splenic Tumour.**

By FRANK KIDD, F.R.C.S.

E. R., AGED 57, referred by Dr. Morton Mackenzie, of Dorking, June, 1911.

History : For the last six months the patient had noticed gradually increasing pain in the left hypochondrium, shooting from thence into the left groin. The pain is sharp and comes on three or four times a day quite suddenly, lasting for about a minute. It is more often felt in the daytime than at night. It bears no relation to food, or to the action of the bowels or to micturition. The patient has had to lie in bed at night on her left side with her legs drawn up. Three months

ago she woke up in the night with the pain more severe than usual and was taken with severe bouts of vomiting. By the next morning all the symptoms had disappeared again. Three weeks ago she first sent for her doctor. While out walking she had been seized with a terrible pain in the left hypochondrium whenever she drew a deep breath. She felt hot and sick and vomited once or twice. She went home to bed, where she stayed for a fortnight with high fever (temperature 104° F. highest),



E. R., case of splenectomy for hypertrophy of spleen. Left kidney filled up with collargol. Skiagram shows outline of normal kidney and pelvis, which proved that the tumour in the left loin was not renal.

and *pain in the left shoulder-joint* higher up than her usual pain. Her doctor noticed a lump in the left hypochondrium and sent her up for diagnosis when the fever left her and she was fit to travel. For years she has had "bilious attacks," that is to say, she wakes up one morning with a headache, vomits and retches, and is like this for two or three days.

Examination: The patient does not look wasted or anæmic, nor is the skin pigmented. The heart and lungs are healthy and the urine is normal. There are no enlarged lymphatic glands. There is no œdema and no ascites. Abdomen: There is a well-defined tumour in the left hypochondrium, which moves down with inspiration from under the shelter of the ribs. It is firm and solid, and there is resonance in front of and below it, and dullness over it and over the ribs in its neighbourhood. The liver is not enlarged.

I made a note, "This tumour is not malignant nor is it a collection of pus. I think it is either a swelling of the left kidney from stone or hydronephrosis, or it is due to the matting of adhesions round the spleen and stomach. There are certainly adhesions pulling on the left leaflet of the diaphragm, as I have learnt (*vide infra*) that pain beneath the left side of the diaphragm is referred to the left shoulder-joint."

In order to determine the nature of the tumour a catheter was passed up the left ureter and 8 c.c. of colloid silver injected. A skiagram taken under these conditions showed that the kidney, pelvis and ureter were normal in size and outline.

On June 18, 1911, I opened the abdomen along the left linea semi-lunaris, and found that the tumour was an enlarged spleen adherent by dense adhesions all over its diaphragmatic surface to the diaphragm. These adhesions were tough and contained no dilated veins. The spleen had to be peeled off the diaphragm by the finger, after which it was easy to isolate the pedicle. This was ligatured by three interlocking silk sutures and the spleen removed. Half a pint of sterile parolene was poured into the cavity left by the removal of the spleen with a view to preventing the formation of fresh adhesions. The wound was united with chromic catgut for the muscles and peritoneum, and silkworm gut for the skin. The spleen weighed 7 oz., and its outer surface measured 13 cm. by 8 cm.

Dr. Turnbull, the pathologist, reported that microscopically the sections are those of normal spleen, the condition being therefore merely one of hypertrophy of the spleen.

The wound healed by first intention, but the patient's convalescence was marred by a sharp attack of pneumonia at the left lung base which lasted some weeks, and left her very weak and complaining of pain in the side for some months afterwards. Her doctor, however, reported (October, 1911) that she had recovered completely and had had no more pain or inconvenience.

In my opinion this case was one of "hypertrophy of the spleen."

My reasons for saying so are as follows: The naked-eye appearance was simply that of an enlarged spleen. The microscopical examination showed no departure in structure from that of the normal spleen. No other cause could be found to account for the enlargement.

Laspeyres<sup>1</sup> has recorded sixteen operations with three deaths on cases of "Simple Hypertrophy of the Spleen." The ætiology and pathology are unknown and there are no characteristic blood changes.

There are three reasons why these cases came to be operated on: (1) The inconvenience and pain caused by the enlarged organ; (2) undue mobility and rotation of the pedicle; (3) the fear that the enlarged spleen might be a primary malignant tumour.

I read my own case as follows: A primary hypertrophy of the spleen occurred which led to undue mobility of the organ. The severe attacks of pain were caused by rotation of the pedicle, and the last one set up an attack of local peritonitis under the left side of the diaphragm which resulted in the formation of adhesions between the spleen and the diaphragm. The pain in the left shoulder-joint caused by adhesions beneath the diaphragm is of great interest. Some years ago I was operating on a man for ruptured gastric ulcer under stovaine spinal anæsthesia. The analgesia was complete, except when I passed my hand up under the left side of the diaphragm to explore the fundus of the stomach. As I did so the patient cried out, "You are hitting me in the left shoulder." I presume that the pain is referred from the left phrenic nerve, which arises from the third and fourth cervical and communicates with the fifth cervical to the suprascapular nerve, which arises from the fifth cervical and supplies a twig to the back of the shoulder-joint.

I have known a pain in the right shoulder-joint be felt by those who are suffering from right-sided subdiaphragmatic adhesions due to gall-bladder or liver trouble, or even to subdiaphragmatic abscess. It is a fact of considerable interest and value and one that deserves wider recognition.

<sup>1</sup> *Centralb. f. Grenzgebiet. f. Med. u. Chir.*, 1904, vii, p. 132 (quoted by Moynihan in "Keen's Surgery").



**Excision of the Spleen for Splenic Anæmia.**

By J. HUTCHINSON, F.R.C.S.

J. C. WAS one of a family of seven children, all the others being strong and healthy. He was always delicate, and at the age of 7 was admitted into the London Hospital, under Dr. Kidd, for lobar pneumonia. His spleen was then found to be enlarged and tender. Four years later he was again in the hospital for splenic anæmia, the spleen extending as low as the umbilicus as a firm, elastic lump. He was then a small and thin child, complaining of pains in limbs and abdomen, vomiting at times, and with loss of appetite. He was very thirsty. A systolic bruit was heard over both the apex and base of the heart; this had been noticed at the time of his previous admission but was then less marked. He had diarrhoea but no pyrexia, his weight was only a little over 3 st., a very light one for his age—11. He was much troubled with cough. There was a strong history of phthisis in the family, but the patient showed no definite signs of it, and in particular no enlarged lymphatic glands. The liver was of normal size. Examination of the blood showed deficiency of red corpuscles, 2,750,000 per cubic millimetre, and of hæmoglobin (45 per cent.), but no excess of white cells (3,400 per cubic millimetre). Seven months later he was readmitted under Dr. Kidd, as his health had steadily deteriorated, and for the first time hæmatemesis had occurred. On January 2, 1912, he vomited a lot of blood, and again on January 5 ("4 pints of bright red blood"). There was now constant pyrexia (100° F.) in the evening, his pulse-rate ranged from 100 to 120, and his respirations were about 24. He was very anæmic; the blood count gave a similar result to that made before, but the red corpuscles numbered less (2,100,000 per cubic millimetre), and the hæmoglobin was only 30 per cent. The white corpuscles were 3,800 per cubic millimetre, of which 63·5 per cent. were polynuclear neutrophiles and 23·5 small lymphocytes. One striking feature in his condition, besides the anæmia and great enlargement of the spleen, was his torpor. He was always sleeping, and when roused showed no interest and was fed with difficulty.

It seemed certain that without operation he must die; probably another attack of bleeding from the stomach would carry him off.

Dr. Kidd and Dr. Robert Hutchison both advised splenectomy, and did not consider the heart condition negated this being attempted. Accordingly on February 7, 1912, I removed the spleen, the patient being anaesthetized with ether by Dr. Ashley Daly. A 4-in. incision in the left semilunar line, with another running at right angles backwards from the centre of the vertical one, gave excellent exposure, the two flaps being held aside by suture retractors. The blood was very thin and watery, and great care was taken to secure all the splenic vessels close to the hilum of the spleen by ligature before division. It should be mentioned that before the operation three doses of  $\frac{1}{120}$  gr. of strychnia and 3 oz. of brandy had been given. During the operation 30 oz. of saline were infused into a vein of the arm. The amount of blood lost was only trifling, and there was no shock except when the splenic ligaments were drawn upon. He bore the operation, which lasted about an hour, much better than I had expected. The severed muscles were brought together by buried kangaroo tendon sutures. The condition of the liver was investigated; it was firm, had a rounded edge, and was slightly cirrhotic. A full examination of the spleen was made by Dr. Turnbull; it will suffice to say that it showed a firm hypertrophy of the whole organ without any signs of inflammation.

The boy made an excellent recovery, and the rapid improvement in his physical and mental condition was most satisfactory. He became bright and cheerful, lost his pallor, and in the course of a few weeks looked quite a different child. Examinations of the blood (which were all made by Dr. Panton) fully bore out the good results of the operation. Two months after it the number of red blood corpuscles had increased to nearly 5,000,000 per cubic millimetre—that is, nearly double the number before; the hæmoglobin increased to 65 per cent., and the white corpuscles to 9,400 per cubic millimetre (three times the previous number). The boy is now, a year after the operation, in excellent health.

#### DISCUSSION.

Sir JOHN BLAND-SUTTON: As far as I can remember, the question of splenectomy has not been discussed in the Medico-Chirurgical Society during the last quarter of a century. In 1888 Sir Spencer Wells<sup>1</sup> recorded the details of a case in which he operated on a young woman for the removal of what was thought to be a large ovarian cyst, but it was a large displaced spleen. The patient recovered, and I know that she was alive and well four years later.

<sup>1</sup> *Med. Chir. Trans.*, 1888, lxxi, pp. 255-63.

At that date surgeons were beginning to realize that the removal of a leukæmic spleen was the most fatal operation in surgery, a lesson they took a long time to learn. A careful study of the literature relating to the removal of leukæmic spleens which I made twenty years ago convinced me that no patient survived such an operation. Since that date matters have changed. Splenectomy for wandering spleen, and certain non-leukæmic examples of splenomegaly, can be undertaken with the same safety as ovariectomy, and it is easy to collect from periodical surgical literature a hundred successful cases. Twenty-five years ago we began to realize the diagnostic importance of the microscopical features of the blood, and some excellent work has been done by this means in disentangling the various kinds of enlarged spleen inseparable by mere histological methods. When, after careful choice of cases, surgeons made splenectomy a success, pessimists admitted the surgical brilliancy of the results, but urged the importance of time to prove the ultimate success of such enterprises. Time has admirably vindicated the activity of the surgeon in regard to the spleen. During the last twenty years I have removed several wandering spleens, a tuberculous spleen, one torn in halves, and one traversed by a bullet; also enlarged spleens associated with anæmia, and two examples of splenomegaly complicated with what is known as acholuric jaundice. I have followed closely, some for many years, eleven spleenless patients; four of them submitted to regular blood examinations and I satisfied myself that for the first few months after splenectomy there is a diminution in number of the corpuscular elements of the blood, a condition which follows any serious operation. Apart from this, there is nothing to indicate that a patient is spleenless. In order to emphasize this, I may mention that in 1895 I removed a big spleen from a little girl on account of splenomegaly associated with anæmia. The child was 5 years of age, and is, I think, one of the youngest patients on whom splenectomy has been performed. That girl has become a healthy, attractive woman. She is now aged 23, and works as a compositor in her father's printing works. Through the kindness of Mr. Roger Hutchinson I am able to show a photograph of the patient and her sister. This is a good proof that the removal of the spleen in childhood in no way interfered with growth and development. There is one matter connected with splenectomy which deserves mention. It is often stated that after the removal of the spleen some patients complain of pains in their limbs, especially in the thighs, and that such symptoms are accompanied by thirst, restlessness, and fever. Gradually these symptoms subside. It has been imagined that, after removal of the spleen, the red marrow takes on the function of the ablated organ, and the symptoms just detailed are caused by the readjustment of the physiological machinery concerned in the production of blood corpuscles. I have never been satisfied with this explanation. It is mere surmise. The symptoms mentioned above are consistent with infective trouble about the stump. The only experience I have had of these symptoms after splenectomy occurred in 1906. I had removed a large wandering spleen from a woman, aged 33; after the operation she had fever, restlessness, and acute pain for several days in the

thighs, but on the twelfth day a large quantity of pus was discharged from the bowel due to an abscess, connected in all probability with the pedicle, bursting into the colon. All trouble ceased in a few hours. The woman recovered and is to-day in good health. Infection of the pedicle is a recognized danger, and a remarkable example was recorded by McGraw in 1888.<sup>1</sup> He removed an ague-cake from a woman, and her convalescence was unsatisfactory; nearly a year later she had hæmoptysis, and, during a fit of coughing, spat up the connected loops of silk used for the pedicle. On the whole, it is more reasonable to attribute the symptoms to infective changes in connexion with the pedicle rather than to supposititious compensatory changes in the red marrow.

Mr. Kidd suggests an important extension of splenectomy—namely, the removal of the spleen for enlargement of this organ secondary to interference with the portal circulation. This is a matter of some importance, for when a person has profuse hæmatemesis associated with an enlarged spleen it is difficult to determine the source of the bleeding. The following case illustrates this: A nurse, aged 26, suffered for six years from recurring attacks of profuse hæmatemesis associated with a big spleen. The bleeding was attributed to a gastric ulcer, and the amount of blood this nurse vomited in some of the attacks was so great that the red corpuscles of her blood were reduced to 662,000 per cubic millimetre. Gradually the corpuscular elements would increase until they reached the proportion of 3,200,000 per cubic millimetre. This always indicated that hæmatemesis was imminent and it invariably happened in a few days. The patient knew when to expect an attack, and eventually died after a profuse hæmatemesis in 1895. At the post-mortem examination the spleen contained two pale infarcts and weighed 33 oz.; the splenic vein was large enough to admit the index-finger; it contained pouches near the spleen, but at its junction with the superior mesenteric vein was blocked by an organized thrombus. There was no lesion in the stomach to account for the bleeding. This nurse was sent to me in 1895 from Australia for splenectomy. In the light furnished by the post-mortem examination, splenectomy would have been a justifiable proceeding. The great attention which is now being devoted to splenic enlargements in that conglomerate group covered by the term "Banti's disease" may help us to distinguish, clinically, hæmatemesis due to thrombosis of the splenic vein from gastric hæmorrhages associated with cirrhosis of the liver. The improvement in the results of splenectomy during the last twenty years is encouraging, and the careful selection of suitable cases based on thorough blood examination is surely leading to an extension of surgical interference in diseases of the spleen.

Mr. F. F. BURGHARD and Dr. G. A. SUTHERLAND reported the after-history of two cases of splenectomy for splenic anæmia. The disease in those cases was of the family type, a sister in the one case having died of splenic anæmia,

<sup>1</sup> *Med. Rec.*, New York, 1888, xxxiii, p. 709.

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and the father and uncle of the second case had enlarged spleens and anæmia. A full report of the cases will be found in the *Proceedings*, 1911, iv (Clinical Section), pp. 58-70.

The first patient, a female, was now aged 20, and the spleen was removed seven years ago. She was a well-grown and well-nourished girl who had been in service for some years. She presented no symptoms referable to the absence of spleen, but suffered at times from the effects of a cardiac lesion, which dated from an attack of rheumatic fever in childhood. A blood examination made this month (May) gave the following result: Red blood cells, 4,740,000 per cubic millimetre; white blood cells, 7,000 per cubic millimetre; hæmoglobin, 98 per cent.; colour index, 1; poikilocytes, none; nucleated red cells, none. Differential count (400 cells): Polymorphonuclears, 76·5; small lymphocytes, 19·0; large lymphocytes, 2·75; hyaline and transitional, 1·0; eosinophiles, 0·25; mast cells, 0·5; total 100. There was no palpable enlargement of any lymphatic glands.

The second patient, also a female, was now aged 9½, and the spleen was removed three years ago. She was well grown and in good health. There had been no recurrence of any of the former symptoms, such as pallor and breathlessness, and the patient was leading the ordinary life of children of her age. A blood examination made this month gave the following result: Red blood cells, 4,510,000 per cubic millimetre; white blood cells, 12,500 per cubic millimetre; hæmoglobin, 88 per cent.; colour index, 0·98; poikilocytes, none; nucleated red cells, none. Films showed a rather large number of blood platelets. Differential count (400 cells): Polymorphonuclears, 41·5; small lymphocytes, 38·75; large lymphocytes, 12·25; hyaline and transitional, 2·75; eosinophiles, 4·25; mast cells, 0·5. The superficial lymphatic glands were not enlarged.

As regards these two cases of splenic anæmia, it would appear that the splenectomy has proved a radical cure. It may be stated definitely that the grave and progressive symptoms which were present before the operation disappeared completely very soon after it, and that there has been no recurrence of any symptoms of disease at periods of, in the one case seven years, and in the other three years.

The PRESIDENT (Mr. G. H. Makins, C.B.) exhibited a girl, aged 9, whose spleen had been removed fifteen months previously for the treatment of so-called splenic anæmia. She had suffered with subcutaneous hæmorrhages and copious hæmatemeses. The patient was now in good health with a normal blood count. An extraordinary post-operative leucocytosis followed the splenectomy, although the wound healed without any obvious signs of infection. Two days after the operation the number of leucocytes, which had never exceeded 3,000, rose to 43,000 per cubic millimetre, and the number only slowly fell, 12,000 being counted on the seventh day.

**A Case of Lieno-testicular Band or Ligament.**

By J. HUTCHINSON, F.R.C.S.

It is well known that small accessory spleens are occasionally met with, as a rule below the main or parent organ. They have been found along the greater curvature of the stomach or in the neighbourhood of the kidney. Their most frequent site is, I think, close to the hilum of the spleen, and here they cannot be said to possess any importance, either physiological or pathological. They may be pedunculated and project into the peritoneal cavity. In the present case, which is possibly unique, a long rounded band containing splenic tissue ran through the peritoneal cavity to the left inguinal region, passed down the canal and adhered firmly to the testicle. As it was quite free from adhesions, except to the two organs referred to, it might readily have caused intestinal obstruction. Its accidental discovery during the course of an operation occasioned much surprise and doubt as to its nature.

A boy, aged 12, came under care for a hydrocele of the left side which seemed to communicate with the peritoneal cavity but could not be emptied into the latter. The hydrocele was bilocular, and when it was opened a firm rounded band was seen to be attached to the body of the testis, which lay at the bottom of the scrotum and was atrophic. The band was moniliform, the enlargements having a purple colour, whilst the rest of the band was white and elastic. Traction on it proved that it passed upwards the whole length of the inguinal canal so as nearly to block a narrow aperture into the abdominal cavity. The band was quite free from the spermatic cord, and it evidently was connected with some viscus high up in the abdomen. I decided to follow it up through an incision in the left linea semilunaris, and found it amongst the intestines reaching all the way up to the left pouch of the diaphragm. Here it was thicker but still rounded, and it finally ended at the hilum of the spleen, being about 12 in. in length. Its upper attachment was secured by a ligature and both band and atrophied testis were then removed. The two wounds, in the groin and abdominal wall, were then closed and a radical cure obtained. Section of the purple nodules in the band under the microscope confirmed the diagnosis that they were splenic in origin.

It is obvious that whatever view be taken of the origin of so strange a band, the connexion between the spleen and left testis must have been formed at an early period of intra-uterine life. Presumably it developed when the testis lay close to the kidney, and as the former descended the band was gradually elongated and drawn down into the scrotum. It is, however, remarkable that the testis was not hindered in its descent, and the fact that it ever reached the scrotum testifies to the power of the gubernaculum testis, as was first pointed out by Mr. Curling. Some writers—e.g., Quain—discredit the idea that the muscular fibres of the gubernacular cord draw down the testis, but an active traction of this kind seems to me necessary to overcome the resistance of an elastic and firm band of the nature met with in the present case.



## Surgical Section.

June 10, 1913.<sup>1</sup>

Mr. G. H. MAKINS, C.B., President of the Section, in the Chair.

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### Retroperitoneal Rupture of the Duodenum.

By R. LAWFORD KNAGGS, M.C.

THE group of cases that it is proposed to consider presents features both in its clinical aspects and operative difficulties that make it one of the gravest consequences of abdominal contusion.

Traumatic rupture of the intestine has of late years attracted very considerable attention and been the subject of various interesting papers, but it is upon rupture into the peritoneal cavity, which is the form usually met with, that attention has been largely concentrated; and though retroperitoneal ruptures have been recorded and tabulated in statistics, their consideration seems to have been neglected, probably because of their relative infrequency.

Retroperitoneal rupture—if we distinguish this accident from sub-peritoneal rupture—can only occur in the duodenum and in certain parts of the large bowel, but owing, no doubt, to the position of the duodenum it is commonest in that portion of the gut. It is unnecessary to do more than refer to the fact, usually emphasized in papers dealing with traumatic rupture of the bowel, that the duodenum, owing to *its fixed position in front of the spine*, is particularly prone to rupture in severe abdominal contusions. But the disposition of the serous membrane in connexion with it ensures that ruptures of the anterior surface shall communicate with the general peritoneal cavity; whilst those on the posterior surface shall open into the retroperitoneal connective tissue.

<sup>1</sup> Provincial Meeting held at the General Hospital, Birmingham.

As the posterior wall, being without a peritoneal covering, will be weaker than the anterior, it might be supposed that it would be more liable to rupture, but statistics show that anterior ruptures opening into the peritoneum are more frequent than retroperitoneal ruptures, so that probably some other factor comes into play. Possibly the explanation may be found in the fact that the retroperitoneal tissue permits more freedom of movement to the posterior surface than the peritoneal covering does to the anterior, so that the former is able to slide out of danger more readily when the compressing force is applied.

Distinction should be made at the outset between a retroperitoneal rupture and a subperitoneal, or partial rupture of the bowel where it is covered by the serous membrane. In the latter instance, if the rupture becomes complete by the giving way of the peritoneal coat the ordinary form of intraperitoneal rupture results, even though the onset of the clinical symptoms of that condition may be delayed, and the fulminating character of the resulting peritonitis prevented, by the formation of limiting adhesions. But it may also happen that the peritoneal covering in such a case may be stripped up by the exuding bowel contents until the retroperitoneal space is definitely opened, and so the subperitoneal injury would become a retroperitoneal aperture. And it is conceivable that in such a case the peritoneum would also give way and both retro- and intraperitoneal extravasations might occur together. Lastly, the rent in the bowel may be so considerable that both the peritoneal and retroperitoneal surfaces may be torn open. In such a case the onset of acute symptoms resulting from the flooding of the peritoneum with duodenal contents would be rapid, the time intervening before operation would be short, and the retroperitoneal extravasation would be slight and not widespread.

From this it will be readily understood that between very definite examples of intra- and retroperitoneal rupture there will be intermediate cases whose clinical course may be out of the ordinary, but in which the post-mortem appearance may fail to show clearly the exact condition produced by the accident.

The importance of the retroperitoneal form of rupture of the duodenum was impressed upon the writer by two cases which came under his care within a comparatively short period. Three features were indelibly fixed in his memory by those cases: (1) The difficulty of coming to an early conclusion that the abdomen ought to be opened; (2) the absence of peritonitis; and (3) the widespread character of the retroperitoneal extravasation. These and other points will be discussed more in detail after the cases have been described.

*Case I.*—Retroperitoneal rupture of the duodenum at the junction of the second and third parts; operation; lesion not found; death.

A. B., aged 24, was struck by another player's knee in the region of the umbilicus in a football match on the afternoon of October 30, 1909. He was "knocked out" at the moment by the injury, and vomited, but he recovered sufficiently to go home by tram, accompanied by a friend. He had pain on the right side of the abdomen from the time of the accident, and during the night vomited everything he took. He was admitted to the Leeds Infirmary on Sunday afternoon (October 31) with a rigid abdomen, especially marked on the right side. There was tenderness in the right lower quadrant, and the liver dullness was present. There was also dullness in the right loin and in the right iliac region, and a fluid thrill could be obtained. Pulse 120, respiration 28, temperature 99° F. He was much troubled with hiccough, and there was marked leucocytosis. He did not look very ill, but he felt so. Soon after admission the abdomen was opened and a considerable quantity of dark-coloured fluid was evacuated. There were some flakes of yellow lymph here and there, and on the outer side of the cæcum and ascending colon were some whitish oedematous patches under the peritoneum. On turning up the transverse colon a curious yellow patch was found near the duodenal jejunal flexure. It was evidently subperitoneal, and was more suggestive of fat necrosis than anything else. The stomach, duodenum, and small and large intestine were all examined, and were apparently normal, but when the coils of small intestine were pulled up out of the pelvis a dark area, suggestive of gangrenous retroperitoneal tissue, was found over the pelvic brim. There was no general peritonitis, and the abdomen was closed without the cause of the trouble being found, or even suspected. Two hours later the patient died from increasing toxæmia and heart failure.

*Necropsy:* The stomach was enormously distended with dark fluid which owed its colour to intense bile-staining and not to blood. At the upper end of the mesenteric attachment there was some emphysema. The peritoneum over the brim of the pelvis had a cushion-like feel, and the same condition was present over the right kidney. Near the appendix the peritoneum was bright green, and on cutting into it bile-stained material oozed out. The same material was found to occupy the right iliac fossa tracking upwards to and around the right kidney. It also passed across the middle line into the pelvis. Mixed with it was some pus in bright yellow flakes which were visible through the peritoneum here and there as spots simulating fat necrosis. This retroperitoneal effusion extended as far as the duodenum and round the pancreas, and was ultimately traced to a large hole in the most dependent part of the duodenum. The hole was the size of a threepenny piece, and the contents of the duodenum had been extravasated without tearing of the peritoneum. The small intestine was distended with gas and bile-stained material for some distance below the rupture. The other organs called for no comment.

*Case II.*—Retroperitoneal rupture of the duodenum; first part; operation; suture; death.

J. P., aged 20, was struck by another player's knee in the umbilical region during a football match on the afternoon of November 26, 1910. There is no record of his condition immediately following the injury except that he was carried off the field. He was admitted to the Leeds Infirmary later in the day, and had passed urine in the interval. When seen at night, except that his lips were very pale his appearance did not suggest a grave injury. The pulse was 80, respirations 32, and temperature 97.8° F. The abdomen moved slightly on respiration; liver dullness was present. There was no distension, no certainty of any free fluid, and pain was not a prominent symptom. Soon after admission he vomited some brown, watery fluid. November 27: During the night he had only a very little sleep, and at 7 a.m. vomited some dark, watery fluid which gave a positive reaction to the blood test. He had now recovered the colour in his lips, and did not look very ill. Abdominal respiration had improved but was not yet satisfactory. The pulse had slowly risen from 80 to 108, temperature 99° F., respirations 28. There was a suspicion of some fluid in the abdomen, but there was no shifting dullness: concentrated urine had been passed several times. His chief symptom was thirst. At 4 p.m. the abdomen had definitely the aspect of commencing peritonitis; the pulse was 120; he had vomited twice some bile-stained fluid, and there was a moderate leucocytosis. He agreed to an operation at once, though he did not seem to think he was very ill. At 5.30 p.m. the stomach was washed out and a large quantity of very dark fluid evacuated. When anesthetized (ether) a median incision was made and eventually extended from above the symphysis almost to the ensiform cartilage. A quantity of dark, watery fluid escaped from the lower abdomen. The great omentum was turned up, and the small intestine was rapidly examined from the cæcum to the jejunal flexure. Close to the cæcum some bubbles of gas were noticed beneath the peritoneal covering of the end of the ileum. There was no general peritonitis. The cæcum and ascending colon were collapsed and thickened and raised up upon a swelling in the right renal fossa, which suggested blood or inflammatory effusion. Turning the omentum down, the pyloric extremity of the greater curvature of the stomach and the adjacent part of the transverse colon were obscured in an infiltrated mass in which there was evidently a good deal of blood. The edge of the liver was adherent to these parts by recent lymph, and when raised up a rounded area of white translucent peritoneum pushed forwards by a collection of gas was seen close to this infiltrated mass and just below the first part of the duodenum. The peritoneum was incised in this translucent area, and a rush of rather offensive gas followed. A quantity of dark fluid, evidently containing bile, also escaped. The retroperitoneal cavity from which the gas and fluid had come, extended outwards and downwards beyond the limits of the finger, and evidently a considerable quantity of fluid had collected in it. On enlarging the opening made in the peritoneum a rent was exposed in the lower circumference of the duodenum

about 1 in. from the pylorus, and by hooking the finger into the pylorus the parts were brought down into view. The rent involved nearly half the circumference of the lumen and occupied equal parts of the anterior and posterior surfaces. It was closed by a continuous suture through muscular and mucous coats. Great difficulty was experienced in dealing with the upper part of the posterior portion of the rent owing to the difficulty of recognizing the edges of the torn bowel in the dirty condition of the surrounding parts, and of bringing them into position owing to the rottenness of the inflamed tissue, and the thickening and stiffening due to the inflammatory infiltration. When the opening was closed Lembert sutures were added, but the placing of these on the posterior surface was almost a matter of guesswork. Owing to the condition of the patient, arrangements for drainage had to be made as quickly as possible. The retroperitoneal space was drained by a large tube with a wick brought out through the abdominal incision. Another tube was brought through the right flank to drain the right kidney pouch, and a third tube drained the pelvis. The wound was then closed. The patient was transfused during the operation, and after operation put on continuous rectal infusion. November 28: He had no sleep during the night, and there was no vomiting after the operation. He seemed more comfortable and felt better, but his pulse and temperature continued steadily to rise (pulse 144, temperature 104° F., respirations 44). He became delirious and died at 6.40 p.m., twenty-four hours after the operation.

Necropsy: There was adhesive peritonitis over the dome of the right lobe of the liver and in the right subhepatic pouch, but the rest of the peritoneum was free. Behind the hepatic flexure of the colon was a large, rounded swelling as big as half a large coco-nut. Above it reached to the posterior surface of the liver, but below it did not extend quite as low as the cæcum. An incision into it showed a purulent infiltration of the retroperitoneal tissue in front of and around the right kidney. Its covering was the posterior parietal peritoneum, and on turning the ascending colon towards the middle line it made a prominent swelling in the right kidney pouch. The leak in the duodenum had been completely secured and withstood a considerable pressure of water.

It is generally accepted that the symptoms due to a rupture of the bowel may not necessarily develop till some time after the injury, but when the interval is considerable it is attributed either to the small size of the rupture and the consequent difficulty of extravasation, or to the empty condition of the intestine. But had rents as big as those met with in these two cases opened directly into the peritoneum and the same amount of intestinal contents been poured *into* the peritoneal cavity instead of *behind* it, could it be doubted for a moment that symptoms of a most acute character would have rapidly developed and have left no question as to the urgent need for exploration?

How, then, is the unconvincing character of the symptoms in the early stages of these retroperitoneal ruptures to be explained? There can be no hesitation in ascribing it to the fact that peritonitis does not set in for a considerable time—not until leakage from the retroperitoneal extravasation takes place into the peritoneum—possibly by rupture of the stretched membrane; or through natural channels, perhaps by back-flow.

It would be waste of time to discuss the variations in the symptoms which after an abdominal injury may make the surgeon hesitate to decide to explore. There is no class of case in which the responsibility of the decision weighs so heavily. Probably every surgeon approaches them in the first instance with the mental question, Ought this abdomen to be opened at once or not? The consequences of delay *may* be so serious; yet the majority of such cases recover if left alone. But the record of the particular group that is now being discussed shows that the surgeon is very apt to err when he meets them and to delay the exploration which, if it is to be of use, should be performed at the earliest possible opportunity.

The outstanding features of these cases, however, may be studied with advantage.

#### (I) RETROPERITONEAL EXTRAVASATION OF DUODENAL CONTENTS.

The most interesting, as well as the most important, is the retroperitoneal extravasation of duodenal contents. In both cases it was a very striking phenomenon. The character of the extravasation is best appreciated if it is investigated after death. An abundant dark bile-stained fluid permeates the retroperitoneal connective tissue on the right side of the spine. It accumulates in the vicinity of the right kidney, chiefly in front, but also passing behind it. Upwards it strips the peritoneum off the lower part of the diaphragm behind the posterior surface of the liver and as it extends downwards to reach the brim of the true pelvis it spreads outwards over the right iliac fossa. It may pass beyond the brim of the pelvis beneath the peritoneum lining the true pelvis, and even reach the left iliac fossa by tracking across the front of the sacrum. The extravasation, which is obviously largely composed of intestinal and stomach fluids, is mixed with pus. The peritoneum is raised up by it, forming a rounded cushion between the spine and the right loin, tailing off towards the iliac fossa, and on this cushion lie the cæcum, ascending colon, and the hepatic flexure. Over the kidney the swelling presents

on either side of the colon. The peritoneum covering the effusion may be stained yellow, but there may be large tracts of a dark olive-green, or almost black colour, where the subjacent fluid shows through the serous membrane, or where possibly the retroperitoneal tissue is on the verge of gangrene.

The conditions are naturally more pronounced after death than at an operation within a reasonable period of the injury, for a longer time has elapsed and the extravasated intestinal contents and the consequent inflammatory effusion are more copious. Moreover, if the abdomen be opened shortly after the injury it is probable that the amount of extravasation may be so small as to be well-nigh impossible of recognition. This probably explains why such a striking condition has not been fully appreciated during laparotomies, though embarrassing coils of small intestine may interfere somewhat with its ready recognition. Numerous cases of retroperitoneal rupture of the duodenum have been explored and have been closed without detection of the laceration, but even the staining of the peritoneum, which may be very conspicuous when the black tracts are present, has failed to raise a suspicion of the real trouble. (Cases I and VII.) But this is perhaps not to be wondered at, for the most striking appearances may be a considerable distance from the seat of rupture.

The physical sign that this effusion must produce during life will be a right-sided dullness continuous above with the liver dullness. This will gradually increase and will not be a "shifting dullness" (Case I). It is evidently a sign of great value, for by its aid a diagnosis of retroperitoneal rupture of the duodenum was made during life in one case (Case IX). But when it has developed it is practically certain that the patient will be in an almost hopeless state, for the retroperitoneal effusion is the cause of the gradually increasing symptoms of septic poisoning which leads to a fatal termination.

## (II) THE CONDITION OF THE PERITONEUM.

Various conditions may occur: (1) A quantity of dark, bile-stained fluid is often met with; (2) there may be no peritonitis at all; (3) there may be a localized plastic peritonitis in the neighbourhood of the duodenum; or (4) there may be a generalized peritonitis which probably has spread from the local focus.

The fluid, which is found within the peritoneal cavity in considerable quantity, both at laparotomies in an early stage or later at the end of a



case, is usually dark and obviously bile-stained or largely composed of bile. As a rule it is not offensive in odour, but if the patient has survived for many days it may be. There can be no doubt that it finds its way into the peritoneal cavity by filtration or osmosis from the retroperitoneal effusion, but at first it is probably not very irritating or highly septic. In Heelis's case (Case V), "between the colon and the duodenum," where the two were in relation, "there was an oozing of bile-stained fluid through several small holes in the peritoneum" in the immediate neighbourhood of the rent in the bowel; but the point of entry is not usually so obvious.

The absence of peritonitis, or the presence of so slight a degree of it as to be a quite insufficient explanation as a cause of death, has been definitely recorded in a variety of cases, and may be inferred in others. Thus in Heelis's case, already quoted, "the peritoneal cavity contained a small quantity of bloody fluid, and the intestines were not adherent or lymph-coated." In Case X, after sixteen hours there was at the post-mortem "no peritonitis" and "the tissues round the right kidney were partially digested." In Bennett's case (Case VII), at an exploration within (?) the first twenty-four hours "no blood or intestinal contents were found" and the peritoneum of the posterior wall was noticed to be abnormal in colour—slightly yellow. In the post-mortem account, death having occurred more than forty-eight hours after the injury, no mention is made of peritonitis, but "the intestinal contents had passed down along the spine and had reached into the pelvis." Again, in Summers's case of bullet wound of the duodenum (Case VIII), where an anterior perforation was sewn up within an hour, and a posterior perforation was drained from behind, death followed in three days and there was found retroperitoneal phlegmonous inflammation without peritonitis. In Alexander Thomson's case (Case III), which lasted five days, and in which the rupture was plugged by a clot preventing extravasation, there would also seem to have been an absence of peritonitis, the peritoneal cavity containing a small quantity of colourless serum and the bowels presenting nothing worthy of remark on being pushed aside.

On the other hand, in Case XI we are left in doubt how far the peritonitis found after death was the result of operative proceedings or infection from the rupture. Thus at a laparotomy at the end of the first twenty-four hours no perforation was found; the abdomen was sponged out, and extensive drainage arrangements were made, and death having occurred some ten hours later the pelvis was found full of bile-stained fluid and the intestines covered with lymph. In Case II

a localized adhesive peritonitis was found at the operation, and there can be no doubt that in a very short time the peritoneum would have given way under the pressure of the gas behind it and a peritoneal abscess have formed, which, if the patient had survived long enough, would have been followed by an extension of the septic process to the general peritoneal cavity. This is how Dr. Ewart explained the conditions found after twelve days' illness in the St. George's Hospital case (Case IV). Here turbid fetid serum was found in the peritoneum, and extensive recent adhesions around the duodenum walled in extravasated duodenal contents. The intestinal contents had also gravitated in the usual way behind the peritoneum. A somewhat similar explanation might also be offered in Sir Jonathan Hutchinson's case of duodenal rupture, which survived for sixteen days, and is so fully related in his Archives (Case XVI). No retroperitoneal extravasation, however, is stated to have been found, so it would be necessary to assume that the injury was of the subperitoneal variety and that the peritoneum endured sufficiently long to enable a protective peritonitis to prevent the general cavity of the peritoneum being flooded with duodenal contents.

### (III) HÆMORRHAGE.

In one case (Morestin's, Case XIII) the abdomen is stated to have been full of blood, but an intraperitoneal collection, and especially one of such magnitude, is unusual. If it came from the gut there must evidently have been a rent in the peritoneum, but it is more likely that it was due to injury to some intraperitoneal structure. It is more common for blood to be found beneath the peritoneum or in the substance of the meso-colon, mesentery, omentum, or adjacent parts, whither it may have tracked from the wound in the bowel, or have resulted from bruising inflicted by the same force that injured the intestine. The presence of effused blood in the tissues was of use in Case II by quickly directing attention to that part of the abdomen where the mischief was. M. Guibé states that in these cases the surgeon has always been put in a way to a diagnosis by a hæmatoma, or at least an ecchymosis, and on incision of the peritoneum at this point the lesion is always found. Even when the lesion has not been found at operation it has been owing to inattention, or failure to, incise a visible hæmatoma.<sup>1</sup> This no doubt overstates the case, but it

<sup>1</sup> *Rev. de Gyn., Par.*, 1910, xv, p. 369.

is nevertheless an observation of great value from the emphasis it lays upon a very useful sign. But in at least two recorded cases hæmorrhage has given rise to conditions that could hardly have been anticipated. In one (Case XIV) a boy died four days after being run over. After death there was found a submucous rupture of the second part of the duodenum, and a large hæmatoma between the muscular and peritoneal coats had led to obstruction. In another (Alex. Thomson's case, Case III), on the outer side of the descending portion of the duodenum was a well-marked tumour as large as a turkey's egg, which was found to be a large coagulum of blood. This clot was found to protrude into the lumen of the intestine through a rent in the bowel an inch long, and had probably prevented extravasation of its contents. Finally, it may be mentioned that though blood has been demonstrated in the vomit, hæmatemesis is a symptom rarely seen, and of little or no diagnostic importance when it is.

#### (IV) EMPHYSEMA.

It might be expected that this striking sign would be almost constant in these cases, but as a matter of fact, it is not very usual to see it referred to. Probably it is often absent or exists only in situations where it may easily escape notice; otherwise it would be difficult to explain why so many cases have been explored without any suspicion being raised as to the nature of the injury.

It is very unusual for emphysema to be recognized before the abdomen is opened. The most remarkable instance found was the case recorded by Mr. Bernard Pitts (Case VI). In that case emphysema of the abdominal wall was noted, as well as free gas in the peritoneal cavity, to which access had been obtained from the abdominal wall through a rent in its peritoneal lining. In Case I, at the post-mortem examination, emphysema was found at the upper end of the root of the mesentery, but it was not detected at the operation. In Case II, however, at the very commencement of the examination a clue to the mischief was afforded by some minute globules of gas beneath the serous coat of the lower part of the ileum, but it was not till the neighbourhood of the duodenum was exposed that a marked condition of emphysema was found. The peritoneum was pushed forwards by a quite considerable collection of gas, and the silvery appearance produced was a most unusual phenomenon and at once compelled attention.

Emphysema is a valuable sign when it is met with during operation after abdominal contusion, for it points to retroperitoneal rupture either of the duodenum or of the large intestine. And as this form of rupture much more commonly affects the duodenum, suspicion will naturally be directed to that part of the bowel first, rather than to the large gut, in those cases where no obvious mischief is at once apparent, but where gas is noticed behind the serous membrane. But when emphysema is recognized in the abdominal wall, and especially when it is extensively distributed, it must be regarded as a very grave sign, for it will almost certainly be associated with widespread retroperitoneal extravasation of duodenal contents.

#### (V) FAT NECROSIS.

Fat necrosis has attracted attention in one or two cases. Its occasional presence is not a matter of astonishment or of much moment. It may be explained by the escape of pancreatic juice through the rent in the bowel, or possibly by an associated injury to the pancreas itself, produced by the same force that ruptured the bowel.

#### TREATMENT.

It would be a trite remark to say that the key to the successful treatment of these cases lies in immediate and early operation. Pains have been taken to show that in very many of them the signs are at first so slight or altogether wanting that immediate operation would only be carried out if it were the rule to operate at sight upon every case of abdominal contusion. As the larger proportion of abdominal contusions recover without interference, such a rule is inadmissible. Moreover, experience has shown that operation, whether early or late, has not infrequently failed even to demonstrate the lesion. A better road to success consequently would seem to depend upon a clearer understanding of the signs and appearances presented by them.

When surgical interference is required in cases of abdominal injury it would be well to bear in mind that ruptures of the duodenum are not very uncommon, and that a certain proportion of them take place behind the peritoneum; that in the latter variety the signs and symptoms are apt to be very indeterminate, and especially that peritonitis may not develop till a late period. The value of localized ecchymoses or a hæmatoma as aids to finding the rupture should not be forgotten, and

the fact that extensive retroperitoneal extravasation of duodenal contents may be expected to occur and to produce a cushion-like swelling on the right side of the spine, lifting up the ascending colon and cæcum upon it, should be remembered. The importance of even slight evidence of emphysema is hardly likely to be overlooked, but the rôle of the retroperitoneal extravasation in leading up to a fatal toxæmia requires to be fully appreciated. The surgeon who is well aware of the facts will not be likely to operate in a case of extraperitoneal rupture of the duodenum and close the abdomen without finding the rent.

A full knowledge of these details, and especially of the late onset of peritonitis, will help also to clear away the difficulties which cause delay in deciding to operate, and so to prevent a certain loss of time. But when the rupture has been found and dealt with, either by simple suture or, because the absence of a peritoneal coat makes simple suture uncertain, by some more complicated procedure at the discretion of the operator, how is the retroperitoneal extravasation to be treated? It calls urgently for adequate measures, for the cellulitis it produces is the cause of death. To attempt to drain it from the front across the peritoneum is useless. To try to deal with it by a drainage-tube inserted from the loin through a stab wound from inside the abdomen is equally ineffectual.

Probably it may be found that the difficulties are insuperable, but so far as it is possible an attempt should be made to deal with it on similar lines to those adopted in extravasation of urine. The retroperitoneal space might be opened up widely by an incision carried through the parietes, like that known as Morris's incision for exploration of the kidney, and this opening might be enlarged by other incisions carried backwards and forwards at right angles to the main incision at such points as would lead to the most effectual exposure of the infiltrated area. The wound would have to be kept widely open by the help of large drainage-tubes and light gauze packing. No doubt such a procedure is a serious one to adopt at the close of a difficult abdominal operation, but as a fatal issue is certain unless the cellulitis can be quickly relieved its gravity should not prevent its adoption.

*Case III.*—Alexander Thomson. Retroperitoneal rupture of duodenum.<sup>1</sup>

W. S., aged 13, on Monday, August 21, 1854, was standing on a branch of a tree getting fruit when it broke and he fell to the ground with his belly on the branch. When raised he was insensible for a short time, but recovered

<sup>1</sup> *Edinb. Med. Journ.*, 1855-56, i, p. 151.

and appeared to be perfectly well. He walked from Musselburgh to Edinburgh the same evening and returned to Musselburgh the next day, making no complaint whatever. That afternoon he was out playing with his companions on the links. His illness first attracted the notice of his friends on the evening of Wednesday, August 23, when he began to complain of sickness and pain at the right hypochondrium. Vomiting set in late in the evening, with marked pallor and constant desire to go to stool. The bowels had been moved without medicine early on Wednesday afternoon, but from that time no evacuation of the bowels took place. He was brought to Edinburgh on Friday, August 25. Pulse was soft, feeble and rapid. Vomiting continued. No tension of abdomen, which was relaxed and flaccid and without the slightest tenderness to the touch. He only complained of a dull, constant pain under the right hypochondrium at the seat of the recent injury. He died on August 26.

Inspection of abdomen (assisted by Dr. Littlejohn): Peritoneal cavity contained a small quantity of colourless serum. On turning aside the bowels, which presented nothing worthy of remark, the descending portion of the duodenum was found of a brownish colour, and on its outer side there was a well-marked tumour as large as a turkey's egg, which was found to be a large coagulum of blood. The stomach was now opened and the duodenum carefully split along its exterior surface. At the lower part of its descending portion, just as the gut begins to pass transversely, a black coagulum was seen protruding into the cavity of the intestine, and on its removal disclosed a linear rent on the outer and back wall of the duodenum fully an inch in length: on passing the finger through the aperture it was found to lead into the cavity of the large clot which had at first attracted notice. No blood could be discovered in the intestinal canal. The duodenal coats were not softened and gave out no perceptible odour. Along the transverse portion of the gut blood had evidently been extravasated between the mucous and peritoneal coats.

Comments: (1) For two and a half days no noticeable complaint was made. (2) The plug of clot probably prevented extravasation. (Compare the prolonged insensibility in favouring clot formation.) (3) Death is said to have resulted from asthenia, no food being taken for five days before death and the bowels not being moved.

#### *Case IV.—Retroperitoneal rupture of duodenum.<sup>1</sup>*

Surgical Registrar's report for 1877, p. 246: G. W., a carriage examiner, aged 19, caught between buffers of two railway carriages. Admission May 2: Shock severe; abdominal muscles motionless on respiration; great pain over pubes and hypogastrium. May 3: Frequent vomiting; pulse 96, temperature 100° F. May 5: Abdominal distension increasing; pulse 100. May 5 to May 14: Rapid improvement; tenderness and pain became much less; fair amount of liquid nourishment taken. May 14: Severe intermittent pain in

<sup>1</sup> *St. George's Hosp. Reports*, 1877-78, ix, pp. 246, 399.

left side (sudden onset); no vomiting; rapidly increasing exhaustion; death in four hours.

Post-mortem: General peritonitis; intestines matted; much turbid serum; faecal odour; no faeces met with till adhesions about duodenum were disturbed, then deep green faeculent matter welled up. The duodenum was extensively ruptured where it crossed the spine. It involved two-thirds of circumference of the bowel and was very ragged. Around was much faecal extravasation. No statement as to rupture being intra- or extra-peritoneal.

Report of the Curator of the Post-mortem Department, Wm. Ewart, M.B., (p. 399): Retroperitoneal rupture of duodenum. This case, No. 148, was interesting from the position of the wound and from the pathological sequence which led up to death. The patient, a railway carriage examiner, was caught between two buffers and his pelvis fractured. There was great collapse and severe epigastric pain and tenderness. These symptoms lasted as long as the patient's life (twelve days). The autopsy revealed the presence in the peritoneum of turbid, fetid serum and extensive recent adhesions around the duodenum. As soon as the adhesions were disturbed some faeculent fluid escaped possessing the characters of duodenal contents, and the mesentery was seen to be raised into a tumour by a collection of the same material between its layers and behind its spinal attachment. The extravasation was traced to a large lacerated wound involving the posterior aspect of the duodenum. The intestinal contents had accumulated in the position described and had gravitated behind the ascending colon to the region of the caecum where they formed a large collection. Fatal peritonitis had probably resulted from the membrane having yielded at some point under the increasing pressure from behind. It should be added that the abdominal pain had been very much subdued during the tenth and eleventh days, when it suddenly returned and was followed by collapse.

(This extract is given verbatim and evidently refers to the case given in the Surgical Registrar's report on p. 246.)

*Case V.—R. Heelis. Retroperitoneal rupture of the duodenum.*<sup>1</sup>

July 23, 3.30 p.m.: Boy, aged 16, was caught between a post and a tub drawn by a horse, the tub hitting him in the right loin and forcing his abdomen against the post. A bull's-eye lantern was driven against his abdomen in the crush. Three or four hours later, when first seen, he was not collapsed; he had a steady pulse; abdomen was rigid and concave. He had vomited once: no blood in vomit. Opium. July 24: Was found downstairs; had walked down; pulse good; abdomen not distended; vomited during the day, and the following night died comatose thirty-seven hours after the injury.

Post-mortem: Abdomen greatly distended; decomposition advanced. Gas in peritoneal cavity. Peritoneal cavity contained a small quantity of bloody, serous fluid and intestines were not adherent or lymph-coated. The colon,

<sup>1</sup> *Lancet*, 1892, i, p. 191.



where it was in relation with the duodenum, was constricted for 3 or 4 in. and slightly bruised. Between it and the duodenum there was an oozing of bile-stained fluid through several small holes in the peritoneum, and on removing that membrane from the front of the bowel a large rent was revealed at the junction of the second and third portions on the right side of the second lumbar vertebra involving fully two-thirds of its circumference. The edges of the rent were ragged and the bowel was bruised for about 2 in. above it.

Dr. Heelis comments on the slight amount of shock in proportion to the gravity of the injury and to the delay in the setting up of severe general peritonitis. He accounts for this by the rent being retroperitoneal and the peritoneum admitting only of a small and gradual extravasation of bowel contents.

*Case VI.—Bernard Pitts. Retroperitoneal rupture of duodenum.<sup>1</sup>*

E. D., aged 19. Thrown off van, the wheels of which passed over his abdomen. Admitted with shock and feeble pulse. Restlessness. No vomiting, or shifting dullness in abdomen. Later emphysema of the abdominal wall was noted, and free gas in the peritoneum. Median cœliotomy. Mesentery found emphysematous and crepitant. Ascending colon found full of blood. No rent of bowel was found. Shock supervened during operation from which patient never revived. Death occurred in a few hours.

Post-mortem: Emphysema of scrotum and abdominal walls. Rupture of abdominal wall between umbilicus and sternum just to right of middle line. Intestines injected. Rent on posterior non-peritoneal surface of duodenum,  $2\frac{1}{2}$  in. from pylorus, measuring  $\frac{1}{2}$  in. Retroperitoneal tissues on right side full of gas, soft and sloughy; gas had spread from retroperitoneal tissue round abdominal wall to a parietal peritoneal rent to the left (?) of the incision and then became free in peritoneal cavity and thence spread to scrotum along inguinal canals. Right hæmothorax.

*Case VII.—E. H. Bennett. Retroperitoneal laceration of duodenum.<sup>2</sup>*

Man, aged 30, admitted November 24, 1897, after a kick from a horse. One hoof struck him above and to the right of the umbilicus, the other above the iliac crest on the right side. He vomited on his way to the hospital (green in colour) and after admission. No mark on the skin of the abdomen. Temperature  $96.7^{\circ}$  F. Seen by Dr. Bennett the morning after admission; looked drawn and pinched; pulse imperceptible at wrist; lips fairly red. Great pain, vaguely seated in the back; abdomen moderately distended and very hard. Liver, spleen, line of colon and stomach could be mapped out on percussion. Diagnosis at time opposed to intra-abdominal hæmorrhage or rupture of hollow viscus. In the afternoon, reaction being more established,

<sup>1</sup> *St. Thomas's Hosp. Reports*, 1897, xxvi, pp. 100, 366. (Case 102, Berry and Giuseppe's paper.)

<sup>2</sup> *Trans. Roy. Acad. of Med. in Ireland*, Dubl., 1898, xvi, p. 353.

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abdomen was opened. No blood nor intestinal contents found: a little rent in the great omentum. Peritoneum of posterior wall was noticed to be abnormal in colour—slightly yellow. Abdomen closed. Death at midnight on November 26.

Post-mortem: The duodenum where it lies against the spine behind the peritoneum, was ruptured. A rent measuring 2 in. in circumference at right angles to the axis of the intestine existed, and the intestinal contents had passed down along the spine, and had reached into the pelvis.

*Case VIII.*—J. E. Summers, jun. Gunshot wound of anterior and posterior walls of duodenum.<sup>1</sup>

A young man was shot below the twelfth rib, and through outer edge of erector spinæ muscle, the ball coming out  $1\frac{1}{2}$  in. below the juncture of the right ninth costal cartilage and the right rectus muscle. One hour later the abdomen was opened. The bullet had perforated the duodenum and gall-bladder. The wound in the anterior wall of the duodenum was sutured, and so were the holes in the gall-bladder. Owing to patient's condition the posterior wound in the duodenum was dealt with by an incision from behind, and the introduction of a gauze pack. The bullet was found to have grooved the lower pole of the right kidney. Death in three days.

Post-mortem: Retroperitoneal phlegmenous inflammation without peritonitis.

*Case IX.*—Berry and Giuseppe. Retroperitoneal rupture of duodenum.<sup>2</sup>

Boy, aged 11. Run over on May 12, 1897, at midnight. On admission, conscious; no severe symptoms; sick twice. Pulse 110, respiration 26, temperature  $97^{\circ}$  F. At 7.30 p.m., May 13, he became unconscious; pulse 152, thready, respiration 40, temperature  $102.4^{\circ}$  F.; abdomen rigid and tender, dullness on right side continuous with liver dullness above, and extending to the right linea semilunaris in front. Diagnosis of retroperitoneal rupture of the duodenum was made, for as patient was not pale the dullness could not be due to hæmorrhage. Too bad for operation. Death, May 15.

Post-mortem: Retroperitoneal rupture of the duodenum  $\frac{1}{4}$  in. long at the junction of the second and third parts; retroperitoneal tissues infiltrated with pus and intestinal contents; no peritonitis; no rupture of the right kidney.

*Case X.*—Berry and Giuseppe. Retroperitoneal rupture of duodenum.<sup>3</sup>

Man, aged 52. Squeezed between the shafts of a wagon and a wall. On admission, persistent shock; upper half of rectus rigid; tenderness in region of umbilicus, some dullness in right flank; movements not good;

<sup>1</sup> *Annals of Surg.*, Philad., 1904, xxxix, p. 727.

<sup>2</sup> *Proc. Roy. Soc. Med.*, 1909, ii (Surg. Sect.), pp. 1-66, Case 49.

<sup>3</sup> *Ibid.*, Case 118.

sick three times. Pulse 68, temperature 97° F. Watched for a few hours, vomiting continued; rigidity increased, abdomen became somewhat distended, and dullness increased. Laparotomy fourteen hours after accident; drainage; no rupture found; condition too serious to allow continuation of operation. Death two hours after operation.

Post-mortem: No peritonitis; hæmorrhage into mesentery and into transverse meso-colon: tissues round right kidney partially digested; rupture of duodenum 5 in. from pylorus, involving two-thirds of circumference.

*Case XI.*—Berry and Giuseppe. Retroperitoneal rupture of duodenum.<sup>1</sup>

June 25, 1907: An adult man, crushed between the tail-board of a cart and a wall. On admission, abdomen moved little on respiration; considerable tenderness over right rectus over which a hæmatoma could be felt. Liver dullness present; no added dullness; no sickness; pulse 90, temperature 98·6° F.; during night sick several times. June 26: Pulse 120, temperature 100·2° F.; sickness continued; abdomen rigid; liver dullness present. 3 p.m.: Pulse 140, temperature 101° F. Abdomen very rigid and tender; vomit, faecal; dullness in both iliac fossæ. 5 p.m.: Pulse 160, condition otherwise the same; never rallied. 7.30 p.m.: Laparotomy right of middle line; no perforation found; abdomen sponged out; drainage from both flanks and from above the pubes and below ensiform cartilage. Died June 27, 6 a.m.

Post-mortem: Right rectus ruptured; pelvis full of bile-stained fluid; no gas; intestines covered with lymph; mesentery along its attachment to the posterior abdominal wall undergoing fat necrosis; a rupture of the third part of the duodenum behind the mesentery.

*Case XII.*—Burggraeve. *Annales Société Med.*, Gand, pp. 49-50.<sup>2</sup>

A sailor, aged 24, was struck in the region of the liver by a heavy timber which fell. Great pain; hæmatemesis. Death without operation at the end of seven days.

Autopsy: Solution of continuity of the duodenum involving two-thirds of its circumference, 7 cm. from the pylorus. Retroperitoneal effusion.

*Case XIII.*—Morestin. Retroperitoneal rupture of duodenum.<sup>3</sup>

Crushed between two stones (rocks). Laparotomy three hours after accident. Abdomen full of blood; great swelling forcing the ascending colon forward. Incision of peritoneum; evacuation; suture of a very extensive transverse tear—subperitoneal—at angle of second and third portions of duodenum. Death next morning.

<sup>1</sup> *Proc. Roy. Soc. Med.*, 1909, ii (Surg. Sect.), pp. 1-66, Case 132.

<sup>2</sup> Guibé, *Rev. de Gyn.*, Par., 1910, xv, p. 378.

<sup>3</sup> *Idem.*, *ibid.*, 1910, xv, p. 379 (Obs. 38).

260 Knaggs: *Retroperitoneal Rupture of Duodenum*

*Case XIV.*—Berry and Giuseppi: Submucous (partial) retroperitoneal rupture of duodenum.<sup>1</sup>

Boy, aged 15. On June 23, 1894, he was run over at the level of the umbilicus. On admission collapsed, vomited once; no hæmatemesis; no signs of injury. Next day abdominal pain began and vomiting became frequent; pulse rapid and feeble. No operation. Death on June 27.

Post mortem: Submucous rupture of second part of the duodenum. A large hæmatoma between the muscular and peritoneal coats had led to obstruction.

*Case XV.*—Sir J. H. Dickson's case. (?) Subperitoneal or partial rupture of duodenum.<sup>2</sup>

Marine, aged 40. Rupture in four different places of the duodenum within 1½ in. of jejunum. Symptoms came on when straining at stool, and patient died the same night. He had been complaining for some days; had been fighting and drinking three days previously, and while wrestling was thrown with violence backwards on to the breach of a gun. The suggestion is made that the mucous and muscular coats had undergone "ramollissement," and the peritoneal coat had afterwards given way from violence or distension.

*Case XVI.*—Rupture of the duodenum.<sup>3</sup>

First day: Mr. W. received a very severe blow in the abdomen from the knee of a competitor in a football match. Two hours afterwards, eyes sunk and aspect like that of a cholera patient. Second day: He had rallied, and was thought to be better. Third day: Suggested diagnosis, injury to liver with extravasation of blood and peritonitis. He had been continuously sick; abdomen was hard and a little full, and breathing was wholly thoracic. Fourth day: Sickness ceased. Swelling of left parotid began. Pulse and temperature both went up to 100. Fifth day: Left parotid much swollen; right beginning. Sixth day: Both parotids much swollen. Bowels acted sparingly. Seventh day: Improving. Eighth day: A little food allowed; a little sickness at times with green vomit. Abdomen not only distended, but decidedly sunken. Ninth day: Again vomiting green stuff. Temperature normal. Tenth day: Improving, but very restless. Eleventh day: Bowels freely open; better in all respects. Twelfth day: Improving. Thirteenth day: Supposed to be much better; taking food, and no sickness. Fourteenth day: A consultation as to whether he might be removed home; not permitted. Pulse 76. Temperature normal for a week. Abdomen not in the least full, and was handled without complaint of pain; but expression anxious, and cheeks dusky and sunken, and he was still liable to occasional attacks of

<sup>1</sup> *Proc. Roy. Soc. Med.*, 1909, ii (Surg. Sect.), pp. 1-66, Case 63.

<sup>2</sup> *Med.-Chir. Rev.*, 1840, N.S., xxxiii, p. 586.

<sup>3</sup> Hutchinson's *Arch. of Surg.*, 1891-92, iii, p. 97. Specimen, Royal College of Surgeons' Museum (A. 2,376).

pain. Fifteenth day: Worse; more feeble. He still had no distension of abdomen, and took his food fairly well. In the afternoon he became much worse. Temperature 101° F., pulse 120. Respiration thoracic, as it had been throughout his illness. Sixteenth day: He died in collapse.

Autopsy: Universal peritonitis. Intestines everywhere matted together with lymph, much of it sufficiently firm to suggest that it had been present from near the beginning of the case. There was also a considerable quantity of fluid which was bile-stained, but had no faecal odour. No gas in the peritoneum, and nothing that could be recognized as the remains of food that had been taken. On tearing through adhesions and displacing the viscera in front of the duodenum a large cavity was opened which contained a creamy, greenish-yellow fluid, evidently with a large admixture of bile, and communicating with this was a lacerated rupture in front of the gut itself. This laceration had ragged edges which looked sloughy, and it was large enough to admit the end of the finger.

Sir J. Hutchinson remarks that "the conditions made it highly probable, though perhaps not quite certain, that the duodenum had been ruptured in the first instance, and that the case had been throughout one chiefly of effusion of bile into the peritoneum," &c.

#### DISCUSSION.

The PRESIDENT (Mr. G. H. Makins, C.B.) offered to Mr. Knaggs, on behalf of the meeting, cordial thanks for his interesting contribution. The author stated that retroperitoneal rupture of the duodenum was an injury which was not very uncommon, but perhaps most of those present had not had a large experience of the accident. In a twenty years' experience of hospital cases it had never come to his lot to encounter such a case, and certainly in his hospital these cases were not at all common. The only one he knew of, except that of Mr. Pitts, which Mr. Knaggs had mentioned, was a second in which the abdomen was closed without the nature of the injury having been determined. The facts which Mr. Knaggs had set forth plainly showed that a surgeon well acquainted with the signs would not be likely to make the mistake of closing the abdomen without finding the nature and site of the injury. He would say a word about the retroperitoneal extravasation. That was remarkable, because in the case of intraperitoneal ruptures of the small or large intestine extravasation of contents was not a marked feature. It was known that in pathological perforations the extravasation of contents was abundant, whereas in the cases of traumatic rupture of the intestine into the peritoneal cavity the escape of intestinal contents was but small. It was difficult, therefore, to understand why, in retroperitoneal rupture of the duodenum, the extravasation should be so widespread; and apparently the spread was one of considerable rapidity. There was a mechanical factor which might be of some moment—viz., that these ruptures lay over the kidney, which organ moved in sympathy with respiratory excursion; hence

it was possible that this might account for a kind of pump action on the perforation; at least the point was worth consideration. Another point which occurred to him was the resemblance between this extravasation and that which was seen in pancreatitis with rupture of the pancreas. There was the same extravasation of blood and a tendency to early gangrene. The extravasation tended in the same way to run down in the lines of the uncovered part of the colon. Putting aside the question of fat necrosis, which was often so striking a feature when the abdomen was opened for pancreatic cellulitis, the picture which Mr. Knaggs drew closely resembled that found in pancreatitis, and the author had not, perhaps, sufficiently emphasized the fact that when the duodenum was ruptured practically unaltered pancreatic secretion would be poured into the tissues and must play an important part in the nature and spread of the retroperitoneal extravasation.

Mr. J. JACKSON CLARKE said he had had one experience of complete traumatic rupture of the third part of the duodenum in the case of a boy, aged 12, who had been run over. He walked a quarter of a mile to the hospital, not because he felt bad, but because having been run over he considered he ought to go to the hospital. He was said to have vomited immediately after he got up, but on examination of the abdomen the same day nothing definite was found. He saw the patient again on the next day because vomiting had started in the night. He opened the abdomen and made a careful search, otherwise he would not have detected a little discoloration of the front of the vertebral column, below the attachment of the transverse mesocolon. That led him to divide the peritoneum there, and he found the duodenum had been cut across as though with a blunt knife. The extravasation was very slight, which he attributed to the initial vomiting, which he took to mean recovery from a slight concussion at the time of the accident. When he had discovered the exact extent and nature of the injury, the operation had been proceeding some time. In order to obtain room to complete the operation he had to join the vertical incision by another across the rectus at one of the intersecting lines. He joined up the intestines end-to-end by a Connell stitch for the deep layer and Lembert sutures for the superficial, a matter of some difficulty at that depth. He regretted to say the boy went on vomiting, symptoms of intestinal obstruction persisted and he died. If a similar case were to come under his care in the future he would tie up both ends of the intestine, invaginate them, and then do a posterior gastrojejunostomy.

Mr. ZACHARY COPE said he had seen one case of retroperitoneal rupture of the duodenum, which was under his colleague, Mr. Clayton-Greene, at St. Mary's Hospital, two years ago. The shaft of a van struck the patient in the right hypochondrium and for two or three hours there remained doubt as to whether the injury was serious. But the pulse-rate increased by 15 or 20 in an hour or two, and therefore exploration was decided on. On making an incision over the right hypochondrium, retroperitoneal emphysema was

noted. An incision was made on the right side of the ascending colon and a very large rent was found in the second part of the duodenum; consequently Mr. Clayton-Greene slit transversely across the muscles to get plenty of room. The rent was too large to close without narrowing the lumen of the gut considerably. He therefore occluded it and performed a posterior gastro-jejunostomy, as Mr. Jackson Clarke had just said he would do in a further case. For some days thereafter the boy did well, but then he died of pneumonia. Post-mortem examination showed the condition of the abdominal contents to be satisfactory. Mr. Knaggs had stated that if the rents in the gut communicated with peritoneal cavity the symptoms would be more severe. He (the speaker) had seen two cases of traumatic rupture of the jejunum in the last eighteen months, and in both cases the symptoms were not evident for the first twenty-four hours, at least not sufficiently to suggest intraperitoneal rupture. When he was called in there were marked symptoms in one case, but not in the other. He saw one case in consultation with Mr. Clayton-Greene and they both decided that operation was not advisable. But some hours later the man vomited again, and as he also had some local tenderness and rigidity, he (the speaker) opened up and found a ruptured jejunum. He thought the reason was that as soon as the injury occurred there was a paresis of the musculature. The peritoneal coat of the adjacent coils of intestine exuded plastic lymph, and the torn mucous membrane pouted so as to fill the opening in the bowel. Then after a few hours the patient was given some food because he seemed to be better; this excited peristalsis, and the feeble plastic layer which had been formed was broken down by the peristaltic movements. In the retroperitoneal tissue there were no coils of intestine to fence in the injured gut, nor was there any similar exudation of plastic protective lymph, but a virulent cellulitis was immediately set up.

Mr. GILBERT BARLING said the record was very monotonous in one respect, for every case described had ended in death, and he did not think the same could be said of any other abdominal injury. One might rescue the person who had his spleen ruptured, or even one who had his large intestine ruptured—both very bad accidents—whereas all the cases now described seemed to die. That was the certain end unless the nature of the injury was recognized quite early. If these patients had had intraperitoneal ruptures, probably a good proportion of them would have been saved, but as far as could be traced the one symptom which would guide to operation in intraperitoneal rupture was not very marked in these cases. He alluded to the extreme rigidity which almost always accompanied ruptured intestines. He could not call to mind more than one or two cases of ruptured intestine in which extreme, board-like, rigidity had been absent. If he saw a case of severe contusion of the abdomen with such rigidity early in the case, he assumed there was rupture of the intestine; and he had never made the mistake of doing the operation too soon in the presence of that extreme rigidity. But, as far as he had read, those cases of extraperitoneal rupture did not seem to show that



symptom. He would be glad if Mr. Knaggs, in his reply, would say whether the extreme rigidity he had alluded to was present or absent in the cases described. There was no doubt that the admission into the subperitoneal area of damaging fluid like pancreatic juice was a disaster of the first magnitude, and one which it was very difficult to obviate. Its intrusion into that particular layer was of the greatest importance, and unless one could recognize these cases in the first few hours after the injury, he feared the records of such cases would be as bad in the future as they had been in the past.

Mr. JONATHAN HUTCHINSON agreed that the mortality attending this operation which had been described was very depressing; but he would call attention to the fact which was not generally recognized—viz., that almost the same discouraging mortality followed at first the operation for perforating ulcer of the stomach. He believed that the late Professor Mikulicz published the first successful case of that kind, and that authority later collected records of 200 such cases, with only two or three recoveries. Yet one knew that now the great majority of cases of ruptured gastric ulcer recovered. It was through the contribution of such admirable papers as that of Mr. Knaggs that surgeons might expect that in a few years there would be a similar change for the better in the cases described, and that successful operations for it would be recorded.

Mr. JAMES BERRY said he of course hoped that Mr. Hutchinson's sanguine view might be realized in the future, but at present he was, on this subject, a pessimist. A few years ago Mr. Giuseppi and himself had published a large number of cases of rupture of the intestine, and had been much impressed by the uniform mortality from the accident when the duodenum was the seat. He would like to know whether anyone present knew of any case of undoubted rupture of the duodenum which had recovered; he doubted whether such recovery had, so far, ever occurred. There was no doubt, as previous speakers had mentioned, that the only chance of saving the patient was by very early recognition and operation; but the difficulty seemed to be that in the early stages there were so few symptoms of any kind upon which a diagnosis could be founded. He had had the good—or the bad—fortune to have seen several cases of retroperitoneal rupture of the duodenum, and he would like to relate one or two of them, because their recital would help to emphasize some of the points which Mr. Knaggs brought forward in his very interesting paper. He remembered the case of a boy who was run over across the upper abdomen, and was taken to a hospital in London, from which he was sent away, the opinion being that there was nothing serious amiss with him. The boy went home, partook of a good supper, and after the meal complained of a violent pain in the abdomen. He then went to another hospital, where he very soon died, and he (Mr. Berry) had the opportunity of making a post-mortem examination. That was some seventeen or eighteen years ago. The boy had an extensive, almost a complete, laceration of the second part of the duodenum, and there was a small hole in the peritoneum. It was obvious that the peri-

toneum had not given way at first, but that when the stomach was filled with food the peritoneum gave way secondarily, and then for the first time he developed marked symptoms, those of peritonitis. Another case was that of a young man who had been struck in the epigastrium by the pole of a wagon, and was admitted to the Royal Free Hospital under his (Mr. Berry's) care. About an hour afterwards he had a telephone message about the patient from the house surgeon, who said the man had been admitted for the accident, but was not at all bad; he only telephoned because it was a standing instruction that he was to be told whenever any patient was admitted with a history of abdominal injury, however slight the symptoms. The house surgeon added that he did not suppose Mr. Berry would think it necessary to come down to see him. But he did go at once, and found that the patient had very marked rigidity of the abdominal muscles, with pain in the hypogastric region; pulse and temperature were both normal. There was obviously a severe abdominal injury, and not limited to the retroperitoneal tissue. He opened the abdomen immediately, some three hours after the injury, and found not only commencing peritonitis, but extensive and almost complete laceration of the second part of the duodenum. But what struck him most was to see a grey, almost gangrenous condition of the retroperitoneal tissue so soon after the injury. In the same way that Mr. Knaggs described, the retroperitoneal tissue was sloughy and discoloured by hæmorrhage, and evidently it was already partly digested by the duodenal and pancreatic secretion. Recollection of that case made him think that when retroperitoneal rupture of the duodenum occurred there was but little chance of saving the patient by operation even if performed within a very few hours of the occurrence of the accident. In another case which came under his care he sewed up the duodenum, and put in a bone tube, but if he were to have another similar case of extensive rupture he would not make any attempt to join the ends, but would do what Mr. Cope had alluded to—viz., put in a large tube and pack round with gauze, and do either a gastro-enterostomy, or a jejunostomy. He would like to hear opinions as to the best course to pursue when one had opened the abdomen and found an extensive rent in the retroperitoneal portion of the duodenum. One other case that he had seen was perhaps worth mentioning; it was that of a girl, aged 12, who fell on to a door-scraper, and injured the upper part of her abdomen. She was admitted to St. Bartholomew's Hospital under the late Sir Thomas Smith, with the diagnosis of ruptured duodenum. She was extremely ill, with distension of the abdomen and frequent vomiting. Everybody who saw her thought she would shortly die—it was in the days before abdominal section was often performed for such injuries. She remained excessively ill for about ten days, and passed large quantities of dark blood *per anum*, and it seemed fairly certain that she had a ruptured duodenum. In the end, however, she recovered completely, and nobody could say definitely what the injury had really been.

Mr. LAWFORD KNAGGS, in reply, thanked those who had taken part in the discussion on his paper, which he feared must have been regarded as of a desultory character. It was difficult to say anything on the points raised which would make them clearer. The President had commented on the difference between the extravasation which took place in the condition dealt with in the paper, and that met with in ordinary rupture of the bowel. He had himself associated this copious extravasation in the former case rather with the fact that the stomach acted as a reservoir which filled up under certain conditions, not from the mouth, but in some way which he did not think was properly understood. In the second case the boy was brought practically straight from the football field, and before operation a large quantity of fluid was drawn off from the stomach. He had had no fluid by the mouth. The stomach fluid was dark and contained some bile. In the first case, after the operation the stomach was found to be distended with a large quantity of fluid. It probably filled up after the operation; it was not put into the stomach by feeding. When one found three or four pints in the stomach within an inch or two of the aperture in the bowel, it was not difficult to understand how it was that a considerable amount of it trickled through. In answer to Mr. Barling, it would be remembered that the first case was operated upon on admission. The boy had been ill over thirty hours. He recognized that in cases of rupture of the bowel there might be a long period devoid of symptoms. He had himself recorded a case in which symptoms were delayed until the third day. But in the paper he narrated two cases in which the symptoms were very slight at first, and there was no peritonitis in either, and yet in both there was considerable extravasation of bowel contents. In the first of them there was rigidity of the abdominal wall. The second case he remembered well. He went to see it several times in a short period, and the pulse records were taken with great care. It might be asked why he did not operate when the pulse was seen to be increasing. At that time his difficulty was great. Though the pulse was increasing the patient seemed generally better, and he had not that pronounced abdominal rigidity of which Mr. Barling had spoken, and that, so far as he could gather, seemed to have been a difficulty also in other cases. In the case of a severe blow on the abdomen one must remember the question of injury to muscles; sometimes, as all surgeons knew, rigidity might be due to muscle contusion, the patient being unable to move those muscles without causing him pain. Again, if after a time the rigidity became less one was apt to conclude that the intraperitoneal trouble was passing away. This was so in the second case, and hence his difficulty in deciding whether to operate or not. In answer to Mr. James Berry's question, when he was looking up records he did not encounter a single case in which retroperitoneal rupture recovered. Some of the references were in foreign languages which he did not know, but as no recoveries were referred to in the English periodicals, he assumed there were no recoveries.

**Note on an Improved Method of Operation in Dupuytren's  
Contraction of the Fingers.**

By J. HUTCHINSON, F.R.C.S.

I BELIEVE that most surgeons will admit that their experience with operation for this deformity has not been wholly satisfactory. The late Mr. William Adams, before the introduction of aseptic or antiseptic surgery, obtained good results by subcutaneous division of the bands of palmar fascia, but the division had usually to be repeated on several occasions, and prolonged treatment with splints to force the fingers towards a straight position had also to be employed. Such forcible rectification is both irksome and unsatisfactory, especially in the case of working men. The open excision of the thickened bands of palmar fascia has, I think, entirely superseded subcutaneous division, and in early cases has given very fair results. But most patients with Dupuytren's contraction do not come to us early, we have to attempt to straighten fingers rigidly contracted for some years, so much contracted that the terminal digit touches or almost touches the palm. The surgeon may make a careful dissection of the band of palmar fascia and remove every portion of it that he can find; still the finger cannot be straightened completely. The time required for healing of the wound will hinder further measures for rectification, and whatever form of splint be employed there is risk of permanent stiffening of the finger. Moreover, it must be admitted that there is a tendency for recurrence owing to fresh formation of fibrous bands on the palmar aspect of the finger.

I suggest that if we can completely correct the contraction at the time of the first operation, both the risk of recurrence and the necessity for forcible splinting will be much diminished. We see this in the case of torticollis due to shortening of the sternomastoid muscle. When surgeons were content with dividing this muscle they found it necessary to employ cumbersome apparatus for a considerable period after the operation in order to force the patient's neck into a good position, and recurrence was not very uncommon. But it has been my experience as well as that of many others that if an open incision is made so as to expose both heads of the sternomastoid, and if the contracted sheath of cervical fascia be divided carefully as well as the whole muscle, stopping

short only at the internal jugular vein, there is no necessity for irksome traction apparatus, and little or no risk of recurrence.

My contention is that in the open operation for Dupuytren's contraction we do not secure, at any rate in bad cases, complete rectification by dissecting out the palmar fascia, however thorough and prolonged may be the attempt. Of course in old cases the skin itself may be contracted, but even if this is notched transversely and the small gaping wound allowed to granulate, or covered with a graft, this makes little or no difference.

What is the anatomical reason for this partial failure, which leaves the finger still somewhat flexed and apt to become more so? The flexor tendons we may disregard, the contraction cannot well be kept up by them; the reason must be found in the ligaments or the articulations of the finger.

It is necessary first to ascertain which joint of the contracted finger is most involved. As the palmar fascia does not extend normally to the last phalanx, the second inter-phalangeal joint ought not to be much concerned, and I think X-ray examination will bear this out. So far as my present experience goes it is in the first interphalangeal joint that the main obstacle to reduction persists after complete excision of the palmar fascial band. Fig. 1, from an untreated case of Dupuytren's contraction, shows for example the terminal phalanx in a line with the second one, which however at its base is bent at less than a right angle on the first phalanx. In the ring-finger the contraction is *nil* at the last joint, nearly a right angle at the first inter-phalangeal one. In both fingers the metacarpo-phalangeal joint is somewhat less flexed than the first inter-phalangeal one.

In Sir F. Treves's "System of Surgery" (vol. i, p. 29), Sir Arbuthnot Lane, who refers to a paper in the *Guy's Hospital Reports* (vol. xliii), well describes the changes consecutive on the prolonged flexion in Dupuytren's contraction: "As time goes on the articulations of the phalanges and metacarpal bones alter their form, in consequence of the prolonged assumption of the position of flexion; and that portion of the articular cartilage which no longer performs its articular function undergoes degenerative changes. The anterior ligaments of the joints also become permanently shortened, and in very advanced cases afford with the shortened muscle and tendons an absolute bar to the restitution of the finger in the straightened position." He notes later, with regard to operative treatment, that "in long-standing and severe cases even free excision of the contracted fascia, combined with section of the tense

tendons and anterior ligaments of the joints, may be of no use owing to the extensive bony, ligamentous, and other changes."

This was written before the advent of the X-rays, which I think will lead us to place most stress upon the changes in the bones themselves, though doubtless the anterior, perhaps also the lateral, ligaments become shortened. We want more evidence from skiagrams, but it is certain that the head of the first phalanx does become altered in shape in some cases, that part which has ceased to be articular becoming

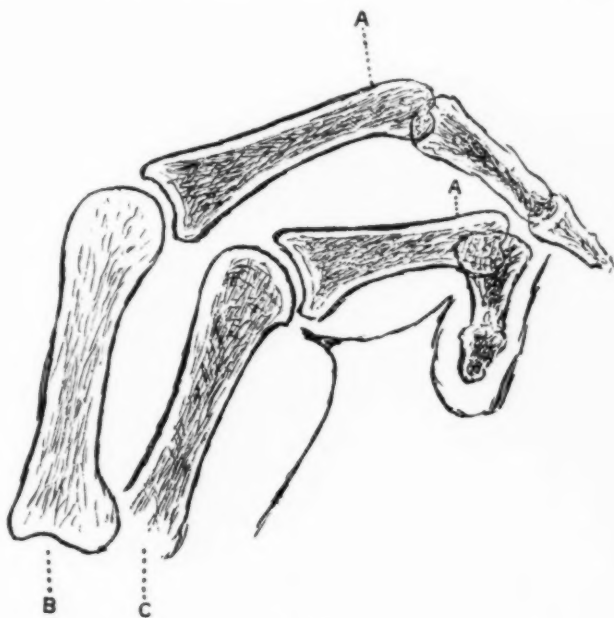


FIG. 1.

Exact tracing of radiograph from case of Dupuytren's contraction. **A**, the level at which the first phalangeal head may be resected; **B**, metacarpal of ring-finger; **C**, metacarpal of little finger. Note that second inter-phalangeal joint is hardly involved in the flexion in either finger.

overgrown and mis-shaped. Such alteration must oppose an obstacle to rectification after the ordinary operation. I do not think that "shortened muscle and tendons" enter much into the question.

The modification I propose is this: When excision of the palmar bands of fascia is found to be insufficient, as it always is in old-standing

cases, the hand should be turned over and the extensor tendon exposed over the first inter-phalangeal joint. This tendon is freed and held aside, or, if necessary, divided (to be sutured again later). The head of the phalanx is then cleared and completely resected at the neck. It will probably be found that this allows of the finger coming straight without tension; by this means the after-treatment will be made easy. Of course, when the head is resected, the anterior or glenoid ligament is divided. It might be objected that removal of this part of bone is

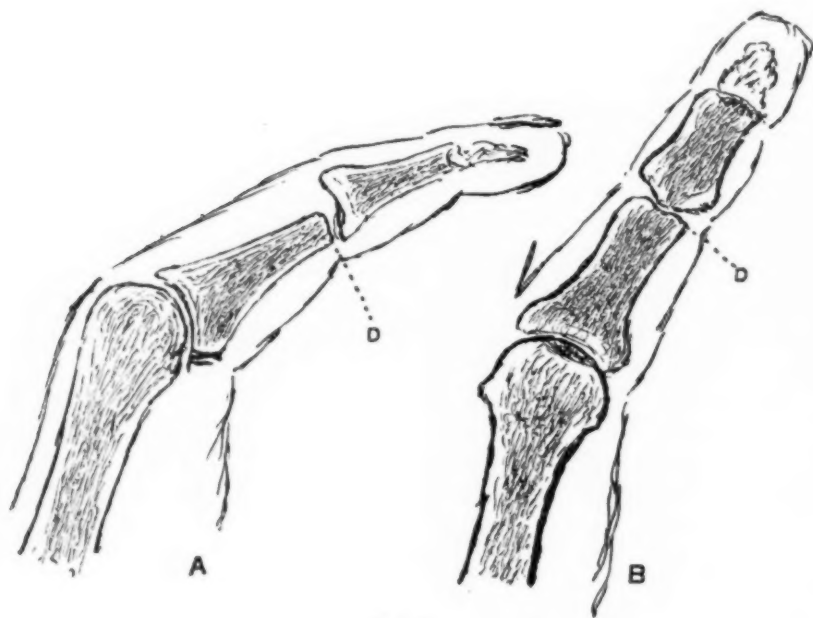


FIG. 2.

Tracing of a radiograph from a case of long-standing Dupuytren's contraction of fourth finger some months after operation. A, side view; B, dorsal view. The palmar fascia has been excised and also the head of the first phalanx at D.

apt to leave a flail-like finger, but my experience has been that the difficulty rather lies in preventing ankylosis. The method resembles that often employed with success in the treatment of hammer-toe. Fig. 2 is from a skiagram of a case treated in this manner; it was taken from an example of severe contraction of the little finger only,



and it shows that the second phalanx is now quite straight with regard to the first.

Doubtless this slight modification in the treatment of Dupuytren's contraction has occurred to other surgeons. My own experience of it is not large, but has been sufficiently encouraging to justify my bringing it to the notice of the Section of Surgery. Further experience, and especially further investigation with the aid of the X-rays, must surely lead us to devise a more perfect treatment for Dupuytren's contraction than is at present the current one. One well-known surgeon told me that he had been so discouraged with it that he had given up operating on this condition.

Mr. J. JACKSON CLARKE said he had been operating on this condition—some of his cases having been severe—for seventeen years, and his experience had not led him to meditate any finger-joint excisions. Mr. Hutchinson had referred to the late Mr. William Adams's work, and had also compared Dupuytren's contraction to wry-neck. Probably Mr. Hutchinson did not intend the comparison as one of a pathological parallel, because wry-neck affected a muscle, whereas Dupuytren's contraction involved the fascia beneath the fat of the hand. The condition affected the foot also. Last week he (the speaker) had a case in which both hands and one foot were affected. An illustrative subject was club-foot. William Adams taught that for congenital club-foot all that is required for its cure is the use of a simple splint for some months, followed by a simple tenotomy, and the application of a simple instrument to the patient's shoe. His experience coincided with that. He had seen cases in which bones had been removed unnecessarily, and one could not produce a perfect foot where oste-ectomies had been carried out. Adams's work on club-foot had never been improved upon, and he would say the same applied to his treatment of an average case of Dupuytren's contraction; if the joints concerned were excised there would never be a result approaching perfection. The subcutaneous sections must be made in the right way and in the right place; not where the skin was attached, but at the intervening portions where it was raised in loose elevations. In very few cases was the skin intimately attached all along. Those few cases only demanded an incision through an open wound; there was no risk nowadays in making an open wound, but the physiological and æsthetic results were not so good as when the old Adams operation was done. The restraint due to the necessary instruments was quite nominal. For six weeks following the operation the patient had a little malleable iron splint, and then an aluminium splint was made. This aluminium instrument was worn, at night only, for a year after the operation. Patients had come back to him after an interval of fifteen years, showing their hands supple and straight, though they had been told by others that it would be useless to operate as the condition would return.

# On the Value of Kangaroo Tendon for Buried Sutures.

By J. HUTCHINSON, F.R.C.S.

OUR late and deeply regretted President, Mr. Clinton Dent, wrote many years ago a study of the use of kangaroo tendon in tying arteries in their continuity. He showed by a series of admirable drawings that the tendon becomes invaded by wandering cells which proliferate, that new vessels are formed between the strands of the tendon, and that the latter becomes ultimately a living piece of fibrous tissue, part and parcel of the host.

I have used kangaroo tendon as a buried suture during the last twenty-five years, and I hope, therefore, that a brief account of my experience with it may prove of interest. As Mr. Dent stated, there is no better material for the ligature of large arteries, but the opportunity for its use in this way occurs but seldom, whereas buried sutures are a necessity in most operations, especially in the radical cure of hernia, excision of the appendix, and a number of other abdominal procedures.

I am well aware that most surgeons employ either silk, catgut, silkworm-gut, or other material for their buried sutures. Probably silk is the favourite of the majority, and certainly the fine Japanese silk is excellent—it can be boiled repeatedly without impairing its strength and it is usually well tolerated or absorbed by the tissues. Even this, however, may irritate, as the following case will illustrate. Some few months after I had excised a breast for cancer the patient returned with a small, hard nodule on the inner axillary wall, which suggested recurrence and was therefore excised. It proved to be merely a ligature of fine silk which had become encapsuled; inflammatory thickening around it had led to a minute cyst in which the loop of silk lay free. Of course this was only one out of many ligatures that had been applied at the operation. When thick silk is used as a deep suture or ligature the risk of its irritating can hardly be denied, however careful the surgeon may have been in his aseptic precautions. Who has not had experience of "radical cures" of hernia in which perfect healing has resulted for a few weeks, to be followed by the development of a small abscess and a sinus which has closed only after extrusion of the buried silk sutures? Silk ligatures applied in pelvic operations have even worked out through the bladder; stout silk used in renal operations has

kept up lumbar suppuration for months, whilst a long series of cases has been recorded in which the great omentum has so resented its application as ligatures that the stump has formed a definite abdominal tumour. Catgut rarely irritates, unless it is over-chromicized, but it is soon absorbed, sometimes too soon, and the occasional dangers in its use as buried material led Professor Kocher to declare, "Away with catgut!" My former colleagues, Sir Frederick Treves and Dr. Arthur Lewers, often used buried sutures of silkworm-gut, which has the advantage of being practically permanent, but I have personally not dared to buy it extensively, being deterred by a few cases of post-operation sinus in which I have had to "dig it out" from the deep tissues.

On the whole my experience with kangaroo tendon has been so satisfactory that I do not wish to find any better material. It is very strong, less slippery and easier to tie securely than catgut, the strands can be readily made of the required size (I think the tendency is to use it too thick), it can be preserved an indefinite time in a strong antiseptic solution, it is well tolerated by the tissues, in fact it becomes a living fibrous structure. In the course of some 800 operations for radical cure of hernia I must have buried many thousands of tendon sutures. Now and then the knots have been imperfectly tied, or from some cause they have given way—every surgeon fails occasionally in obtaining a "radical cure"—but however freely kangaroo tendon has been used, sinus formation has been the rarest possible event. In the worst forms of hernia—large umbilical, inguinal, or ventral—I trust entirely to kangaroo tendon. Take, for example, an umbilical hernia in which there is tension in bringing together the edges of the abdominal aperture. A series of mattress sutures of strong tendon are used to relieve the tension, and a second row of interrupted tendon sutures applied as closely as it is practicable to insert them. In operating on these large herniæ it *may* be advisable to insert silver filigree as urged by some, but I feel sure that anyone who is experienced in the use of kangaroo tendon will but rarely find this necessary.

After suprapubic cystotomy tendon sutures through the bladder wall are safe and satisfactory. For fixing a floating kidney, for tying the renal vessels in nephrectomy, for ligaturing any form of vascular pedicle, I have almost always used tendon. After removal of the vermiform appendix, whether suppuration has existed or not at the time of operation, I have never hesitated to bring the muscular and aponeurotic layers together with fine kangaroo tendon, leaving, if necessary, just

room enough for a drainage-tube. I must own to a feeling that a ventral hernia after these operations is to be sedulously guarded against, that it is both a nuisance to the patient and (sometimes, though not always) a reflection upon the surgeon's methods. This feeling I understand is not shared by all, for a well-known American surgeon recently wrote that in suppurating appendix cases he packed the wound with gauze and "waited for the inevitable ventral hernia." Another surgeon observed that he rather liked a ventral hernia, as it "enabled him to follow up the case." Perhaps this statement was not meant to be taken seriously!

It is a delusion to suppose that tendon sutures when buried in the tissues are rapidly absorbed. I have had the opportunity several times of examining them from one to five years after their insertion—they are easily recognized and microscopic sections prove how well they are organized in the manner already described.

There is never any need to harden the tendon with chromic acid; indeed, they may irritate if so treated. Of course they cannot be sterilized with heat, but it is easy to render them aseptic by soaking in alcoholic solutions of carbolic acid, bichloride or biniodide of mercury, and they can be preserved indefinitely in such a medium.

They are obtained, not from the large kangaroo, but from the small wallaby, of which animal there is an unlimited supply in Australia. Hence the material should be plentiful and cheap, and there is no justification for the price charged by certain purveyors of "sterile ligatures."

Buried sutures are an absolute necessity in most surgical work, and for this purpose I believe there is no material which combines strength with freedom from risk of irritation more than kangaroo tendon.

In sewing up the abdominal wall, it often happens that there is some tension involved in bringing together the divided peritoneum and adjacent fascia, and so one does not like to trust to catgut. I always use fine tendon for this first line of suture; it will hold well, and leaves a smooth peritoneal scar. I also use it for stitching the rectal sheath. Twenty-five years' experience with this tendon has been so satisfactory that it seemed worth while to record it in the hope of inducing other surgeons to try the tendon for buried sutures.

PROCEEDINGS  
OF THE  
ROYAL SOCIETY OF MEDICINE

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VOLUME THE SIXTH

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COMPRISING THE REPORT OF THE PROCEEDINGS FOR THE  
SESSION 1912-13

THERAPEUTICAL & PHARMACOLOGICAL SECTION



LONDON  
LONGMANS, GREEN & CO., PATERNOSTER ROW  
1913

## Therapeutical and Pharmacological Section.

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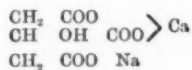
Professor W. E. DIXON, F.R.S., President of the Section, in the Chair.

### The Selective Action of Drugs on Nerve-endings.

By W. E. DIXON, M.D., F.R.S.

## GENERAL OBSERVATIONS.

THE method by which drugs bring about their several effects in the animal body may be of the simplest or most complicated character. The action of strong sulphuric acid in charring organic matter is the same in living and dead tissues, and depends upon the affinity of this acid for water. The astringent action of the heavy metals, and of the drugs containing tannin, is determined by the fact that they combine with, and precipitate, certain protein substances. Other chemical processes of a more delicate nature than the preceding, and which are responsible for the action of drugs, may be exemplified by the action of citric acid, which combines with the calcium in the body, forming the not very soluble salt—



This substance does not ionize so as to liberate the calcium ion, and the specific action of citric acid depends upon its power of removing the calcium ions from the blood.

Many drugs lose their toxicity and their special action in the body by combining with some substance which not only renders them inert but facilitates their excretion. Thus salicylic acid combines with glycocoll, is rendered inert, and is rapidly excreted by the kidneys.

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as salicylic acid. But it is not with these relatively simple chemical changes that I propose to deal but with certain specific effects of drugs. By this I mean that a drug having reached the blood of a living animal selects one or more tissues upon which to exert its action, leaving all others relatively unaffected.

In any consideration of this selective action of drugs on special tissues two important problems must be considered. The first concerns the entrance of the drug into the cell. A drug might reach the blood-stream but for physical reasons be unable to penetrate certain cells in the body and so fail to produce an action on those cells. Tetanus toxin cannot reach the cells of the central nervous system directly through the blood-stream, and there is strong presumptive evidence that this is true also of the alkaloid colchicine.

The well-known views of Overton [68] and Meyer [66] seek to explain the selective action of the indifferent hypnotics and narcotics for the central nervous system, on their relative solubility in brain lipid and insolubility in water. More recently Traube [85] has called attention to the tendency of a good many narcotics to produce changes of surface tension, and suggests that the narcotic action is dependent on this property. This hypothesis does not seem, however, to be sufficiently general, thus the striking relationship which Meyer discovered in the sulphonal series cannot be accounted for by changes in surface tension. Nor do the experiments of Moore and Roaf [67], who attempted to show that chloroform combined chemically with proteins, help much, since they employed a concentration of chloroform which invalidated their experiments so far as any deductions to the animal body were concerned. Nor is there any evidence that these indifferent hypnotics produce changes in the state of aggregation of lecithin or cephalin to account for such a phenomenon.

The evidence points strongly to the view that physical phenomena enter largely into the problem as to what substances shall or shall not be absorbed into living cells. Cocaine, for example, paralyses all nerve-fibres when applied in concentrated solution, yet exerts a selective action when applied in dilute solution, picking out some fibres and paralysing them before or to the exclusion of others; thus the afferent vagal fibres to the medulla are paralysed before the efferent inhibitory fibres to the heart. Now the afferent and efferent fibres are freely mixed up together, so that the cocaine must either penetrate the afferent fibres a little more easily than the efferent or it must have a greater specificity for some fibres than others, after absorption into the

substance of the nerve-fibre [18]. The evidence is strongly in favour of the first view, since a large number of very diverse chemical substances exert an action on nerve-fibres and they all show the same selective action on the afferent fibres, and it is well known that moderate injury to a nerve is more likely to lead to afferent than efferent effects.

A drug, then, having obtained access to a cell, the second problem is the change which it brings about in the cell. In the case of narcotics, which is the example we are considering, we may refer to the hypothesis of Baglioni, who bases his views on the various groups of benzene phenol derivatives. The amount of paralysis produced by these substances varies inversely with the amount of oxygen present in the side-chain, and he concludes that narcotic effects depend on the power to withdraw oxygen from the nerve-tissues, or, in other words, that narcosis is a reduction. Herter has shown that chloroform, ether and chloral diminish the oxidizing capacity of the tissues.

It is, however, with regard to the selective action of drugs on peripheral nervous structures to which I particularly desire to draw your attention, and as most of the hypotheses which have been suggested to account for selective action are based on the supposition that drugs combine directly with some constituent of the cell, it will be well to consider what evidence is available in support of this supposition. In the case of toxins it has been definitely shown first by Wassermann [87] that the cells of the central nervous system which were known to be affected by tetanus toxin anchored the toxin. But in the case of drugs no such clear proof is forthcoming.

Strychnine, like tetanus toxin, has a specific action on the cells of the spinal cord, and several attempts have been made to prove, by methods similar to those adopted by Wassermann for tetanus toxin, that strychnine acts by combining with the spinal cord or with one or other of its constituents. Widal and Nobécourt [88] showed that when a solution of strychnine was added to an emulsion of brain, liver, or kidney, and injected into animals the toxicity of the strychnine was weakened. Von Brunner [8] also comes to the same conclusion and supports the side-chain hypothesis for the action of strychnine. Thoinot and Brouardel [84] mixed strychnine with charcoal, talcum and starch, and on injection have observed a diminution in the effect of the strychnine. The experiments of von Czyhlarz and Donath, who attempt to prove the fixation of strychnine by the tissues, are of little significance to us since their object was to show that the

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tissues of the limb fixed the strychnine, that is, that the fixation was not necessarily specific. The interpretation which they give to their experiments, namely, that the limb tissues can fix strychnine, has been shown by Meltzer and Langmann to be open to serious objections. [14]

Still more recently Sano [79] has returned to the attack; he says that strychnine loses its effect when added to an emulsion of spinal cord and injected into frogs. He determined the amount of strychnine free to act in his emulsions by injecting into frogs and examining the reflexes. Sano concludes that strychnine is especially neutralized by the white substance of the cord, less strongly by the anterior portion of the grey matter, and still less by the posterior.

Strychnine mixed with an emulsion of cord shows no evidence of having entered into chemical combination, since it can still be separated from the mixture by means of the ordinary solvents for alkaloids. In this respect, then, it behaves quite differently from tetanus toxin. Furthermore, all these observations which we have mentioned can be more readily explained in another way than by supposing that the strychnine enters into some form of combination with the spinal cord.

Dixon and Hamill showed that when strychnine is mixed with milk, or even with a suspension of chalk, a diminution of toxicity is seen, quite comparable with that obtained when it is mixed with an emulsion of spinal cord. They produce evidence to show that emulsions of spinal cord added to solutions of strychnine do not interfere with the specific effect of the alkaloid, except by delaying its absorption, and they point out that spinal cord emulsion in no way differs from other tissue extracts in neutralizing the effects of strychnine. Similar effects to these can be obtained with curare; if a dose of curare sufficient to produce motor paralysis be mixed with an emulsion of spinal cord and injected into a pithed frog, the paralysis may never occur, not because the curare is destroyed or combined, since it retains its properties if the fluid is filtered, but on account of delayed absorption. No positive evidence is forthcoming from these experiments that strychnine has combined with the spinal cord emulsion. It must be accepted, then, that when the crucial experiment of the side-chain hypothesis is applied to vegetable drugs—strychnine, morphine, cocaine, and the like—it yields negative results. It has been urged that the chemical combination is of such a delicate nature that the methods described are not valid; to which a reply might be made by asking the

further question, then why are they valid in the case of toxins? Koch and Mostrom [39] conclude from their experiments that the central nervous system, especially the cord by its high phosphate content, is enabled to pick the strychnine from the blood-stream on account of the affinity of the lecithin and kephalin for the strychnine as compared with serum albumin, but there is no evidence that this attraction of the strychnine by phosphatids is other than physical.

It must not, however, be accepted as a general rule that because an alkaloid exerts a specific affinity for a certain tissue it will necessarily only collect in that tissue, though in many cases it undoubtedly does so. Nicotine, for example, exerts its action on nerve-cells when administered by the mouth or injected into the circulation in non-lethal doses; yet Heger and others have shown that it quickly disappears from the blood, and is taken up by the liver, from which it can be obtained by distillation. Indeed, it is now generally admitted that even tetanus toxin may be fixed in other cells besides those on which its activity is most manifest; thus the cells of the liver and spleen, besides those of the brain and spinal cord, fix tetanus toxin.

Many other attempts have been made to show that drugs act by chemical combination, thus Matthews [62] thinks that potassium may combine directly with colloid so that the colloidal complex acts as the anion. Koch and Pike [40] state reasons for their belief that the greater concentration of potassium in the cells of a tissue as compared with the surrounding lymph spaces or serum, can be partly explained by a specific affinity of this element for some phosphatids, especially kephalin.

No conclusive evidence exists, as yet, proving that physiological activity produced by drugs is brought about by a chemical combination between the drug and the protoplasm of the cell; this question will be dealt with in further detail later.

It is, of course, true that some drugs combine chemically with organic constituents of the body, and in so doing lose their specific action, but the combination does not bring about physiological activity, and it is usually a means by which the body diminishes toxicity and facilitates the excretion of a drug.

In the case of the natural hormones of the body, which induce physiological activity, the method of action does not appear to be the same as in the case of the vegetable alkaloids. Elliott [25] showed that so minute a quantity as 0.02 mgrm. adrenalin if passed through the great aerated expanse of the lung vessels survived to influence all

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the systemic vessels, and much of the tissues fed by them, whereas much larger amounts, passed down a single systemic branch vessel such as the femoral artery, utterly failed to reach the general system; from this and other evidence he concludes that adrenalin disappears in the tissues which it excites. Dixon and Hamill showed that secretin is destroyed quantitatively by some constituent of the pancreas, and although it is destroyed also by other tissues the relative rate of destruction is greater in the case of the pancreas. Pituitary extract (posterior lobe), the active principle of which is a much more complicated body, does not appear to follow this rule, as it is said to be excreted in the urine [16].

It will be well now to notice briefly the hypotheses which have been advanced to account for the action of drugs. Biologists until recently have been content to accept the giant protoplasmic molecule of Pflüger as a basis upon which to build: Loew's "*System der Giftwirkungen*" should serve as a warning to all who would build on this speculation. The modern biologist should be content to regard the cell as a co-ordinated system of ferments, which may be influenced by drugs either by a chemical action on the constituents or by influencing the activity of one or more ferments, until such time that some evidence can be adduced in support of the giant molecule.

The first hypothesis is that of Ehrlich [24] who held the view that alkaloids being foreign to the animal body were not capable of combining with protoplasm to form such stable compounds as those formed by toxins, but more recently he has laid stress upon the view that drugs which specifically affect tissues are bound to the protoplasmic molecule by certain atomic groupings which he distinguishes from toxin receptors by the term "*chemo-receptors*." These chemo-receptors are evidently quite distinct from food receptors and it is difficult to regard them teleologically as being pegs specially designed for the physician on which to hang his drugs. Langley's [45] view is much the same as that of Ehrlich: he regards tissues as containing receptive substances with which the drugs can combine, and these receptive substances may be side-chains of the protoplasmic molecule; neither Ehrlich nor Langley gives any idea as to the chemical nature of the receptor. Koch believes that in the living cell two sets of factors must be considered: (1) chemical activities which go on in watery solutions, that is, interaction between non-colloidal molecules, and (2) the control of these by the colloidal aggregates. I suggested tentatively that physiological activity in any tissue may be caused by



the liberation of a specific hormone, and that drugs may act by greatly increasing, or diminishing, the production of these bodies, without themselves necessarily taking part in any chemical change, but acting rather as catalytic agents. These views will be considered in detail under the several headings.

Before proceeding to the study of the selective action of drugs on peripheral nerve structures, it may be noted at once that in all nerve-muscle and nerve-gland structures drugs are known to stimulate the end-organ in two distinct ways. They may, on the one hand, produce effects closely simulating if not identical with the effects of nerve excitation, or, on the other, they may produce a different type of effect which is generally more gradual in onset and more prolonged in duration: paralyzing agents which remove the action of the first group fail to affect that of the latter. For convenience the first group is generally spoken of as acting on nerve-endings and the second group on the end-organs, muscle, or gland.

#### SELECTIVE ACTION ON MOTOR "NERVE-ENDINGS."

A considerable number of drugs are now known which act upon voluntary muscle of vertebrates in such a way that electrical stimulation of the nerve no longer induces contraction: curare is the best known of these, and it will be well to take this as a typical substance. Bernard [4] established its selective action on motor nerve-endings. He showed that after a frog had received a small dose of curare, the motor nerves of the muscles of the trunk and limbs on electrical stimulation ceased to cause muscular contraction though the muscles responded as readily as before to direct stimulation. He showed, further, that the central nervous system, nerve-trunks, and sensory nerves were not decidedly influenced by doses of curare sufficient to paralyze motor nerves. Bernard referred the seat of action to the nerve-terminations and clearly appreciated that he was dealing with a specific selective action. Bernard's work was extended and amplified by Virchow [86], Kölliker [41], Pelikan [70], Eckhard [22], Funke [28], Pflüger, and many others. After the discovery of nerve-endings, which were regarded as different from the nerve-fibres from which they arose by division, it was natural enough that the seat of action of curare should be referred to these. Bernard regarded curare as acting first at the periphery of the nerve-endings and gradually spreading upwards and affecting the trunk, and a paralyzing action on the nerve-trunk was also described by

Kölliker and Kühne [42], although the latter observer in later experiments could not convince himself that curare in large amounts had any effect on nerve-fibres.

Up to this time, then, the simple view was universally accepted that curare paralysed the anatomical nerve-endings in striped muscle. Kühne (loc. cit.) first produced clear evidence which showed that no such simple interpretation was possible. He worked with the sartorius muscle of the frog and showed that the irritability of the different parts of this muscle varied with the number of nerve-endings: it was most irritable at the point of entrance of the nerve and least at the ends where nerve-endings were absent. He then showed that a paralysing dose of curare did not abolish this difference in irritability. Therefore, either curare does not act upon the nerve-endings, or if it does the varying irritability of the muscle must be due to inherent differences in the muscle cells. Kühne decided against the latter view, because he found that if he passed a constant current through the nerve to the muscle, with the positive pole near the muscle so that the end of the nerve was thrown into electrotonus, the irritability of the muscle became the same throughout. He felt then compelled to conclude that curare did not act upon the nerve-terminals, although after the administration of very large doses he admits that the whole nerve-ending might be paralysed, with which view Sachs [78] agreed. Kühne's experiments were amply confirmed by Pollitzer [74], who also supported Kühne's views and who suggested that the action might be on the cement substance of the last node.

Nevertheless, Kühne's work never really changed the older and simpler view held by pharmacologists that it was the nerve-endings which were paralysed by curare. Within the last fifteen or twenty years, however, new facts have been constantly brought to light which cannot be explained by the old supposition, that the nerve-ending is a simple structure which can be excited or paralysed by drugs as an entity.

Langley [46] has published a series of papers on the action of nicotine, a drug which in large doses paralyses, according to the ordinary acceptance of the word, the motor nerve-endings. If 1 mgrm. of nicotine is injected into the vein of an anaesthetized fowl, the hind limbs become stiff and remain in this condition for about half an hour. After the injection of from 10 to 15 mgrm. the motor nerves become paralysed to electrical stimulation: nevertheless, further injections of nicotine still cause some muscular contraction. This fact might seem

to suggest that nicotine exerts a double action, on the nerve-endings and upon the muscle. If this supposition is correct then curare should not eliminate the effects of nicotine, but Langley has shown in the fowl that a sufficient dose of curare annuls the contraction produced by a small dose of nicotine and diminishes that caused by a large amount. From this it is argued that if nicotine excites the muscle, curare must depress it and that the two drugs act upon the same tissue.

In order to investigate further the seat of action the method has been adopted of cutting the nerve, allowing sufficient time for it to degenerate, and repeating the experiments on the denervated muscle. Langley examined the gastrocnemius muscle of the fowl six, eight, twenty-seven, thirty-eight, and forty days after section of the external peroneal nerve which innervates it, and obtained effects with nicotine almost identical with those on normal muscles: the nicotine contraction was reduced by curare. His conclusion is that nicotine, and therefore curare, acts upon the muscle. Now nicotine and curare have very little influence on the normal contraction of muscle to direct stimuli, so that the contractile substance can hardly be the seat upon which these drugs act. Therefore a third tissue must be invoked which can be neither contractile muscle substance nor yet nerve. Langley calls this a receptive substance. When working with adrenalin Brodie and Dixon [6] adopted the term "neuro-muscular junction," and a similar term has also been used by Elliott ("myo-neural junction") to express something upon which drugs acted which was neither muscle nor yet nerve. One might regard Langley's receptive substances as identical with the myo-neural junction, except that he believes that his receptors are acted upon by drugs with which they combine chemically. I am not aware of any direct evidence supporting this idea, nor does Langley bring forward evidence in its support.

It is frequently assumed that nerve-endings do not degenerate along with the axis cylinder after section of the nerve. It may be well before proceeding further with our argument to note the histological evidence of this. These observations are not numerous, but they are in agreement. Sokolow [81] investigated degenerated nerves in the gastrocnemius of the frog, using the gold chloride method. Cipollone [10] also used the frog's gastrocnemius. He confirmed Sokolow in the main, and describes a formation of deeply staining particles which disappear in later degenerations. Hoffmann and Bass [34], by the methylene blue method, found no nerve-endings forty to sixty days after section of nerve. Langley [47] used various muscles of the frog and compared

the two sides, normal and denervated. He found that the nerve-endings of the sartorius ceased to stain thirty-six days after cutting the nerve. Huber [36] investigated the interosseus muscles of the rabbit by the methylene blue method, and Tuckett the nerve-endings in the flexor profundus muscle of the pigeon. All the results tend to show that after section of a motor nerve to striped muscle the anatomical nerve-endings first undergo granular degeneration in two or three days and they disappear in from three to six days.

Nerve-endings are said also to exhibit histological changes when under the influence of curare, and this has been used to support the nerve-ending hypothesis. Kühne [43] states that curare causes the living nerve-endings in the muscle of lizards to become more distinct. Herzen and Odier [33] find that curare causes the hypolemmal fibres of the frog to become varicose, and they state that granular changes occur not only in the nerve-endings but in the axis cylinder. Miura asserts that prolonged curare poisoning in the frog causes a dwindling in the size of hypolemmal fibres. In view of these diverse observations they cannot at present be regarded as decisive. But in spite of the evidence that nicotine, curare, and other drugs to be described presently, do not act upon the anatomical nerve-endings, and which for the time being we may accept as valid, the upholders of the nerve-ending hypothesis can still fall back on the ultra-terminal nerve-fibrils as the seat of action of drugs (Ruffini and Apáthy [77]), or they may place the action at the myo-neural junction, also a hypothetical structure not partaking either of the anatomical nerve-ending nor yet of the contractile muscle substance, a view which may imply a continuity between nerve and muscle; and Pflüger [71] has again brought the theory of continuity to the fore.

Keith Lucas [59] has employed a method for differentiating the various substances in muscle by determining for each substance the curve relating the liminal current strength to the current duration. Experiments made on the pelvic end of the sartorius muscle of the toad yield always a simple curve with constant form. This he regards as belonging to an excitable substance ( $\alpha$ ) contained in the muscle-fibres. In the sciatic nerve-trunk a simple curve is found belonging to a substance ( $\gamma$ ) whose excitatory process is more rapid than that of  $\alpha$ . When experiments are made on the middle region of the sartorius a variety of curves are found consisting of  $\alpha$  and  $\gamma$  curves, and of a curve more rapid than either ( $\beta$ ) together with their various combinations. In the pelvic region of the sartorius stimulation affects only a single

substance ( $\alpha$ ) which is distributed throughout the whole length of the muscle-fibre and is not affected by curare. The nerve-trunks contain a substance ( $\gamma$ ) whose excitatory process is more rapid than that of  $\alpha$ : it is frequently excited when the electrodes are applied to the middle region of the sartorius muscle, and is no longer in functional connexion with the muscle after weak doses of curare. In the region of the sartorius, in which the nerves end, is the  $\beta$  substance with its extremely rapid excitatory process: it remains in functional connexion with the muscle after enough curare has been given to sever the functional connexion with  $\gamma$ . The experiments show clearly that there must be three different substances in the nerve-muscle system, each of which directly or indirectly can excite contraction.

I shall now consider the action of nicotine and curare in the frog. If the muscles of *Rana temporaria* are exposed in succession, and nicotine applied to a small spot with a fine brush, twitchings and slow tonic contraction occur, but in different degrees, in different muscles, and, as one would expect, larger amounts are required to effect this in the winter than in the more active summer frog. This seasonal variation bears many analogies to the inhibitory action of muscarine on the frog's heart, which can be obtained with minute doses of the drug in the summer animal, but in the torpid winter animal much larger doses are required to produce the same effect. After the application of nicotine to the isolated frog's muscle, or the exposed muscle in situ, different kinds of contraction can be seen, which vary in different muscles. Langley mentions three: one confined to the neural region, one in the general muscle substance, and a nicotine rigor.

Now it has been shown by Mays [64] that the nerve-endings in the sartorius of the frog occur chiefly in a band near the entrance of the nerve, and in another band one-fourth to one-third from its upper end, and it is just at these spots that the muscle is most irritable, and that small drops of nicotine produce their maximum or sole effect, and so constant is this action in the sartorius and other muscles that Langley has suggested that the position of the nerve-endings in the superficial fibres of a muscle can be ascertained by observing the points which respond most readily to dilute nicotine. The twitchings are produced only in the region of the nerve-ending, and the slow tonic contraction is produced more readily in this position than elsewhere. If the circulation is stopped, or if the muscle is fatigued, the twitchings caused by nicotine are abolished before the slow tonic contraction. The sartorius placed in 0.01 to 0.1 per cent. nicotine often retains for some time two

local swellings in the regions which contain the majority of nerve-endings. Besides this stimulating effect Langley noticed that the height of contraction obtained by stimulating the muscle with sub-maximal induction shocks "is reduced by nicotine."

It will be remembered that Kühne showed in his classical experiment with the gracilis muscle that if a stimulus is applied to a peripheral nerve branch supplying a portion of a muscle, the impulse might pass centrally along the branch, and then peripherally by another branch causing contraction of another portion of the muscle. The local application of nicotine to muscle never causes contraction of any kind, remote from the spot touched. This evidence is adduced by Langley in support of the view that the anatomical nerve-endings are not excited by nicotine.

Langley and others have performed experiments in which various muscles of the frog were immersed in nicotine solutions, and as the conclusions drawn from these experiments are important they warrant further description. It is well to be clear on one point that the application of dilute nicotine solutions causes contraction in the neural region of the muscle. The use of stronger solutions or even dilute solutions for a more prolonged period causes a rigor presenting many of the characteristic features of the caffeine rigor. Thus 0.25 per cent. nicotine-Ringer causes a shortening of the muscle both in and outside the neural region, and Langley regards this as an action on the general muscle substance in contradistinction to the action of more dilute solutions affecting the neural region only, which he places on receptive substance. This rigor is largely dependent upon continuous immersion in nicotine; if the nicotine solution is run off there is a slight diminution in the contraction, although nicotine still adheres to the muscle. If the nicotine approximates to 1 per cent. the muscle will enter into complete rigor involving its death. When a muscle is placed in 0.01 per cent. nicotine for two or three minutes, then washed with Ringer's fluid, and left in Ringer's fluid, the contraction remains complete for several hours. This Langley regards as strong evidence that dilute nicotine does not stimulate either the nerve-endings or the myoneural junction, but forms a chemical combination with some part of the muscle substance. It is not clear whether Langley considers that this condition of contracture is distinct from the muscle twitches produced by the punctiform application of nicotine, and which are antagonized by curare and fatigue. It is clear, however, that the contracture is an effect on the contractile substance, but no evidence is



forthcoming to show that the nicotine enters into chemical combination with the muscle. In the case of caffeine and other substances which produce contracture and twitchings of an analogous nature the change is brought about by the conversion of myosinogen into myosin, probably as the result of lactic acid formation. Without entering into the merits of the question, it seems to me that there is at least as much evidence that this alkaloid acts by facilitating certain forms of ferment action, particularly oxydases, as that it enters into direct chemical combination. Nor is there any evidence that nicotine rigor, in any degree, is different from that produced by caffeine, and until evidence is forthcoming to the contrary, it is surely simpler to regard this type of rigor as not essentially different from that caused by other drugs.

If the sartorius muscle of a frog is soaked in 0.001 per cent. curare for fifteen minutes, and is then removed to a bath containing 0.01 to 0.1 per cent. nicotine, contraction does not usually ensue, but with a slightly more concentrated nicotine solution contracture is at once set up and the action of curare in antagonizing this effect increases with the strength of the curare. Langley's conclusions from experiments of this nature are that curare in all cases puts an end to the stimulating action of nicotine, and that curare has little or no effect upon the state which is caused by stimulation, that is, the contraction; from such experiments he concludes that curare paralyzes the receptive substance, but in the percentages used is without effect on the general muscle substance.

Boehm showed that a number of ammonia bases, including nicotine in dilute solution, caused tonic contraction of the isolated gastrocnemius of the frog. If the muscle was, however, first immersed in 0.1 per cent. curare-Ringer contraction was not observed, but if the muscles were removed from a previously fully curarized frog they still exhibited the tonic contraction on placing them in the nicotine solution, and he concludes that curare in nerve-paralysing doses does not antagonize this form of nicotine contraction. Langley showed that Boehm's results only held for certain strengths of curare and nicotine. After the injection of a sufficient dose of curare the gastrocnemius does not contract with nicotine up to 0.1 per cent., but does with 0.5 and 1 per cent. This does not, however, affect Boehm's position that if the dose of curare is just sufficient to paralyze completely the motor nerves, then nicotine has the same action as before. In this connexion it is well to note Boehm's [5] work further. He showed that the gastrocnemius of a frog takes up from a bath of 0.1 per cent. curarine solution many



times the amount of drug that is necessary to produce the maximum curare effect on motor nerve-endings: he found also that the muscle gave up the curarine very slowly, and it was not possible to remove it completely. These experiments certainly look as if curare, in the doses necessary to produce paralysis of the motor nerves, does not affect the nicotine contraction, but that when larger doses of curare are injected, or when the gastrocnemius is soaked in curare, some degree of antagonism ensues as the result of some further action of the curare not directly associated with the motor paralysis. It is well known that by exciting a motor nerve to muscle, fatigue is set up which is referred to the nerve-endings, since impulses no longer pass from these to the contractile substance of the muscle. Slight poisoning with curare causes the fatigue to appear much sooner, and the larger the dose of curare the earlier the fatigue, so that it has been said that the production of fatigue is of the same nature as curare poisoning since the two can summate; but even supposing that the paralysed organ and the fatigued organ are one and the same, this does not localize the seat of action.

It is well to point out here that different muscles of the frog react in different degrees to nicotine and curare, and it is not advisable to compare the results obtained by one observer, who may have employed the coraco-radialis muscle with those of another who used the sartorius.

Boehm found in the gastrocnemius that curare sometimes increased the rate of relaxation, but never if the nicotine exceeded 10 per cent. Langley believes that curare always causes relaxation after nicotine if the contraction is being maintained at the time by stimulation of the receptive substance.

Boehm thinks that the muscle tonus caused by the immersion of the whole muscle in the nicotine bath corresponds with Langley's contraction of the muscle of the fowl, and the experiments of Edmunds and Roth [23] certainly support his contention. These observers repeated Langley's experiments on the bird, and showed that the denervated muscle responded with greater promptness and to smaller doses of nicotine than the normal muscle, but that to curare it loses its response at practically the same time as its nerve-ending degenerates, after which time the only curare effect obtainable is a slight alteration in the nicotine curve, which they think may be due to a direct action on the contractile substance proper. The conclusion of Edmunds and Roth, then, is opposed to the view of Langley, which was that curare antagonized this effect of nicotine in the denervated as well as in the normal muscle, and Langley suggests that Edmunds and Roth's results

are due to another factor, a decrease in what may be called the relaxing power of the general muscle substance, and adds that an increase in contracture is a well-known feature of atrophying muscle. It is hard to believe, even bearing in mind this property, that the denervated muscle which is more sensitive to nicotine than the normal, should show practically no relaxation with curare if the nicotine effect is annulled.

The evidence as to the seat of action of curare clearly, then, cannot be regarded as decisive. Langley's view is largely based on the highly controversial evidence that curare has an antagonistic action to nicotine both on normal and denervated muscles of the fowl and frog; and he states that because curare antagonizes the nicotine contractions both in the normal muscle-tissue and in the denervated muscle, that it must therefore act on the same structure as nicotine, a structure which he places in the muscle and terms a receptive substance. Pharmacologists are clear that, in the present state of our knowledge of the structure of such organs as the "nerve-endings," arguing as to the seat of action of drugs from antagonism experiments may be full of pitfalls. Physostigmine, as is well known, causes in mammals fibrillary twitchings of the voluntary muscle which still occur after section of the motor nerves, but not after the administration of curare (Harnack and Witkowski [32]). Pal [69] and Rothberger [76] found that this curare paralysis could be relieved by physostigmine almost completely. These two drugs obviously, then, form an excellent example of mutual antagonism, curare stops the physostigmine twitchings, and physostigmine relieves the curare paralysis. Magnus [61] cut the sciatic nerve in mammals and examined the effect of physostigmine seven, fourteen and eighteen days later, but still found twitchings; after from twenty-seven to thirty-four days, however, physostigmine was without effect, although the muscles still retained their irritability, and this should mean on Langley's reasoning that curare acts on the nerve-endings, whilst if nicotine and curare are employed and the same type of reasoning adopted, the seat of action of curare is found to be peripheral to the nerve-endings on the "receptors of the muscle." Langley replies to this by stating that Magnus deals only with the theory that the specific action of poisons is one on the nerve-endings, and states that Magnus does not consider his theory of the presence of more than one receptive substance in the cell. But Langley himself argues that because nicotine and curare are antagonists both act on the same receptive substance, so that if physostigmine and curare are antagonists, they, too, must both act on the same substance, and therefore, unless curare acts on more than one receptive substance, all three bodies must act on the same.

Rothberger described in 1901 the antagonistic action of both nicotine and physostigmine to curare. Edmunds and Roth conducted some experiments on the antagonistic action of physostigmine and curare, using the fowl anesthetized and atropinized, so that the vagi were paralysed and the characteristic muscle twitchings were absent. They found that when from 2 to 5 mgrm. were injected the tone of the muscle gradually increased, beginning generally about 10 minutes after the drug was given and lasting about ten minutes, but the muscle never relaxed completely. The injection of from 5 to 15 mgrm. curare produced immediate though incomplete relaxation on muscles in which the sciatics had been cut and allowed to degenerate for varying times from twenty-four hours to fifty-three days. Curare antagonizes physostigmine during all the stages of degeneration, removing the contraction (except the condition of contracture). This is different, then, from Edmunds and Roth's effects with nicotine, and clearly disposes of Langley's explanation of the failure of curare to relax the denervated muscle in their experiments, namely, because in degeneration the relaxing power is lost. It is a matter of regret that in these experiments curarine was not used more frequently, and where that was impracticable that the curare was not standardized to show the minimal quantity which would paralyse the motor nerves in a frog of known weight. To speak of a 1 per cent. solution of curare without this information is of little value.

The seat of action of curare in the absence of a crucial experiment must, then, remain unsettled. Much may be said in favour of the view that it paralyses the nerve-endings. Histological observations favour this; the fact that the muscles of a frog completely paralysed by curarine react normally to nicotine (Boehm); the fact that curare has little or no effect on the nicotine contraction in the denervated muscles of the fowl (Edmunds and Roth); and the antagonism experiments of Magnus and others. On the other hand, in favour of the view that it paralyses a more peripheral substance are Kühne's experiment; the fact that large doses of curare prevent nicotine contraction in the frog (Langley); and the fact that curare relaxes the physostigmine rigor in the denervated muscles of the fowl.

It is quite clear that the tonic contractions of muscle which can be brought about by nicotine in the frog and fowl are produced by exciting a substance peripheral to the nerve-endings, and it is certain that in some circumstances large doses of curare show an antagonistic action to these effects; but all we can conclude from this is that under the conditions of experiment curare seems to have a direct action peripheral to the nerve-endings.

Perhaps the most inspiring work is that of Lucas, who has analysed three types of excitable substances found in the skeletal muscles of frogs and toads. The  $\gamma$  no doubt represents the nerve-endings, the  $\alpha$  the ordinary muscle, and the  $\beta$  the myo-neural junction (Elliott, Brodie and Dixon), the receptive substance (Langley), the hormone (Hamill and Dixon). Now, under normal conditions, the nerve impulse must pass from  $\gamma$  to  $\beta$  to  $\alpha$ ; but drugs may take short cuts and influence either the  $\beta$  or the  $\alpha$  directly.

This conception in no way furthers Langley's hypothesis, which is an extension of the side-chain hypothesis of Ehrlich; he regards each drug as having its own receptive substance (chemo-receptor of Ehrlich) with which it is bound by chemical combination. On the other hand, it may express what is meant by a myo-neural junction; and if the  $\beta$  were a chemical substance which under certain conditions could combine with  $\gamma$ , resulting in an extremely rapid excitatory process, it would express the views of Dixon and Hamill. As regards the action of curare, the experiments of Lucas certainly suggest that the seat of action is the nerve-endings.

#### EXPERIMENTS ON THE IRIS.

The mechanism by which drugs influence the pupil, in spite of numerous investigations, is not yet quite clear. The older view was that atropine paralysed the nerve-endings of the motor oculi, and that the pupil dilated because the circular muscle-fibres of the iris having lost their tone, the radiating muscle-fibres were free to act and open the pupil. The proof that atropine affected the nerve-endings consisted in the fact that the post-ganglionic fibres of the third nerve when excited electrically were without effect on the pupil after injecting the alkaloid into the circulation or applying it locally to the conjunctiva. The circular muscle was, however, intact since this would still respond to direct stimulation. Physostigmine was regarded as acting directly on the sphincter muscle because it constricted the pupil after moderate doses of atropine, and it was also supposed to act on the dilator muscle because muscarine causes greater constriction of the pupil than physostigmine. This argument was applied by Harnack and Meyer [31] to pilocarpine, and since this body does not constrict the pupil after moderate doses of atropine they believed that it acted on the nerve-endings only. Harnack thought that large doses of atropine paralysed the muscle of the sphincter as well as the nerve-endings, though Schultz

and others find that the sphincter is excitable even after large doses of atropine.

Roebroeck noticed that after cutting the three long ciliary nerves there was local dilatation of the pupil, and this is considered by Winkler to be due to the long-continued irritation of the cut nerves.

Langendorff [44] showed that after excision of the superior cervical ganglion or section of the cervical sympathetic nerve the paralysed pupil under certain conditions became larger than the control: this he called paradoxical pupil dilatation; and similarly after excision of a ciliary ganglion or after section of the oculo-motor nerve the paralysed pupil was sometimes smaller than the control. The explanation which Lewandowsky [53] gives to this paradoxical dilatation seems the most reasonable: he regards it as due to the increased excitability of the paralysed muscle; and the paralysed muscles unquestionably have been rendered more excitable. The condition is comparable with the increased excitability, to which attention has already been drawn, in the denervated voluntary muscles of the vertebrata. Anderson [1] adopts the same view for paradoxical constriction. He found that in the case of cats in which the ciliary ganglion had been removed or the oculo-motor nerve cut, partial asphyxia caused the paralysed pupil to become smaller than the control; this he thinks is due to the increased excitability of the sphincter: the effect may be evoked by a local stimulus. It is necessary to be acquainted with these so-called paradoxical effects before the effect of drugs on the normal iris can be compared with those on the denervated.

P. Schultz failed to obtain any constriction of the pupil four days after the removal of the ciliary ganglion, even with the free application of 5 per cent. solution of physostigmine to the eye, and he concluded that this drug acted only on the endings of the short ciliary nerves. The experiments of Anderson are by far the most valuable in enabling us to form an idea as to the seat of action of these drugs. He showed that after section of the motor oculi nerve in the skull pilocarpine constricts the paralysed pupil more than the control but physostigmine constricts it less. Both drugs, however, constrict it for a longer time. After degenerative section of the short ciliary nerves physostigmine does not stimulate the denervated sphincter but pilocarpine excites it to an increased and abnormally prolonged contraction. Schultz and Anderson, then, are in agreement that physostigmine acts on the nerve-ending and Anderson believes that pilocarpine acts upon the sphincter muscle. Moreover, after imperfect regeneration of an oculo-motor nerve physo-

stigmine restores the light reflex when it is not to be detected under normal conditions, but pilocarpine has not this effect. Physostigmine does not increase the excitability or conductivity of the short ciliary nerves or ganglia, or of the oculo-motor fibres. These experiments, then, are apparently directly opposed to the views of Schmiedeberg for the seat of action of physostigmine, and of Harnack and Meyer for that of pilocarpine. This illustration affords another example of the necessity for caution when drawing deductions from the antagonism of drugs, especially when the seat of action of neither has been determined.

Ulrich showed that the pupil contracted well after death in an eye which had been kept under the influence of atropine for fourteen days previously, and Placzek also observed that the post-mortem constriction of the pupil is not altered by atropine; Anderson also has described similar observations. Atropine, therefore, does not alter the excitability of the sphincter muscle so far as the products of dyspnoea are concerned.

After section of the short ciliary nerves (Anderson) or the motor oculi (Schiff) and allowing plentiful time for degeneration, these observers found that atropine did not dilate the paralysed pupil further and both pupils were the same size after atropine had been applied to the eyes. It does not appear, then, as if atropine could excite the dilator muscle-fibres to contraction. Nevertheless, atropine prevents the action of pilocarpine on the denervated sphincter, either by acting on the same thing as the pilocarpine, or it may be by introducing a block between it and the contractile portion of the sphincter. So far, then, we have, as in voluntary muscle, three excitable things to consider: (1) The contractile substance excited by the products of dyspnoea and not paralysed by atropine; (2) the substance excited by pilocarpine and possibly paralysed by atropine; (3) the substance excited by physostigmine and lost after degenerative section of the short ciliary nerves. These excitable things present many analogies to the  $\alpha$ ,  $\beta$  and  $\gamma$  substances of voluntary muscle.

Other views as to the mode of action of physostigmine have been suggested by Loewi and Mansfeld [56]. These observers believe that the action consists rather in augmenting the irritability of the terminations of the cranial and sacral autonomic nerves for normally subliminal stimuli than by acting as a stimulus itself. Their reasons for this view are that the effects of electrical stimulation of a nerve are augmented by the previous injection of physostigmine; and injections of physostigmine may not cause an augmentor action without subsequent electrical



stimulation. They explain the numerous exceptions on the supposition of peripheral tone existing in certain organs; but a rule which requires such a proviso in half its applications seems to me of little significance. The increased irritability of a nerve to electrical stimulation is also seen after small doses of pilocarpine and is possibly analogous to the fact that a second or third stimulation of a nerve with a weak current will generally cause an effect better than that caused by the primary stimulus. Moreover, it is difficult to appreciate what is the difference between a peripheral nerve showing increased irritability, and stimulation: are they not in reality degrees of the same effect? Cushny suggests that the increased irritability of the vagus and chorda manifested after physostigmine is really the lower phase of the stimulant action of the drug, which culminates in actual stimulation in more susceptible organs or in more favourable conditions. In this connexion it is well to remember that physostigmine does not increase the excitability or conductivity of the ciliary nerves or ganglia, nor of the oculo-motor fibres, even when they are regenerating, and the work of Anderson on physostigmine shows, therefore, that the impulses imperfectly transmitted by the regenerating oculo-motor fibres are blocked chiefly in the ciliary nerve-endings.

Several weeks or months after removal of the ciliary ganglion and of the ciliary nerves with the accessory ciliary ganglia, the denervated sphincter begins to respond again to physostigmine, yet the light reflex is absent and the ciliary nerves do not respond to stimulation. Anderson nevertheless believes that the response is due to regeneration because (1) the return of response is gradual and at first local; (2) it is absent longer after more complete removal of the ciliary nerves; and (3) it disappears again after a second section of these nerves.

#### SELECTIVE ACTION ON THE CARDIAC VAGUS.

The group of drugs to which I will now call attention produce their effects for the most part in a manner simulating vagal stimulation or depression. Muscarine was supposed by Schmiedeberg and Koppe [80] to cause its effect by stimulating the inhibitory ganglia, and this view was strongly supported by Kobert [38], who found that a dose of muscarine, which will easily cause standstill when applied to the sinus, will not arrest the contractions of the isolated ventricle of the amphibian heart. In accordance with this Pickering [72] found that muscarine is ineffective on the hearts of embryos when they first begin to beat.



Gaskell [29] found that stimulation of the vagus nerve caused an electrical variation of the opposite sign to that caused by a contraction in the non-beating tissue of the auricle of the tortoise. When the sinus of the tortoise is brought to a standstill by the application of muscarine no electrical change is produced in the auricle indicative of the stimulation of inhibitory nerves. He concluded from this that muscarine did not act as an excitant to the inhibitory mechanism, but as a depressant to the motor activity.

Now it has been clearly shown that an important action of a large number of drugs is to depress and, later, paralyse certain nerve-cells in the body. Nicotine and apocodeine will serve as examples of this group, although nicotine differs from apocodeine in that it first excites the ganglion cells before paralysing them. Nicotine then readily paralyses the vagus nerve in the frog, but the inhibitory neuron must still be intact, since stimulation of the sinus venosus still causes arrest of the heart exactly as in the normal animal, the obvious reason being that the current is now exciting the post-ganglionic fibres, and that the nerve-cells occur on the course of the intracardiac vagus. The members of the pilocarpine and muscarine group still act quite as usual even when the ganglionic cells are paralysed by nicotine; they do not act, however, after small doses of atropine. Atropine, like nicotine, paralyses the vagus, but it acts more peripherally, since in the atropinized frog's heart direct electrical stimulation of the sinus is without influence on the rhythm.

Harnack and Witkowski [32] had shown similar facts for physostigmine, that the frogs dosed with this drug responded to weaker electrical stimuli than before; and Winterberg [90] much more recently found that the administration of physostigmine increased the susceptibility of the vagus to both chemical (nicotine) and electrical stimuli.

The view adopted usually is that muscarine, pilocarpine, and physostigmine produce their effects on the heart by exciting some portion of the peripheral vagus mechanism, no doubt largely because the similarity of the two results has suggested an identity of cause. The hypothesis is, however, occasionally disputed, as we have seen from Gaskell's work, and more recently by Matthews [62] and others, so that it may be well to review briefly the evidence upon which it is based.

If pilocarpine stimulates the vagus mechanism, then we might expect to obtain a greatly diminished effect by exhausting these nerve-endings prior to the injection of the drug. On the other hand, it is possible that the vagus might be rendered more sensitive to electrical

stimulation by the injection of small doses of pilocarpine, and that pilocarpine would produce a more profound action after slight electrical excitation of the vagus; all these conditions can be easily demonstrated. So that from a priori reasoning it might be anticipated that if pilocarpine excites the vagus nerve small doses should increase the irritability of the vagus to electrical stimulation, and large doses should paralyse. Langley [48] has shown that this is so for the frog, and Marshall [48] for the mammal.

In the early months of the year during the period of sexual activity of the frog, difficulty in obtaining good inhibitory results from vagal stimulation is frequent. And it may be regarded as a general rule that when faradization of the vagus has little effect on the heart, pilocarpine and muscarine also have little effect, and vice versa; the two methods of producing inhibition are strictly proportional to one another in each frog. The hearts of eels and newts obey the same law. The further question as to whether a submaximal effect by any form of vagal stimulation can be converted into a maximal, cannot be regarded as clear. Jonescu [37] thinks not; Honda [35], on the contrary, finds that muscarine and vagal stimulation can summate.

The evidence, then, clearly points to the fact that these drugs produce inhibition in a manner similarly produced with the inhibition obtained on faradization of the vagus nerve. In the heart it is not possible to produce degeneration of the peripheral inhibitory neurons, on account of intracardiac vagal ganglia, so that no crucial experiment exists showing whether the seat of action of these drugs is on, or peripheral, to the vagal nerve-endings. If, however, it is permissible to judge by analogy with their action on other tissues, we must localize them (muscarine, pilocarpine and atropine) as acting peripherally to the nerve-endings, although closely associated with them on the  $\beta$ . Gaskell's experiments, perhaps, afford evidence in support of this view.

Within the last two or three years considerable importance has been attached to the presence of calcium in peripheral nerve tissues, and in the case of the vagus and sympathetic nerves to the heart it has even been suggested that the effects produced by excitation of these nerves could be explained by changes in the calcium and potassium content. It has been shown that calcium-precipitating substances administered to frogs destroy the vagus inhibitory powers, and Chiari and Fröhlich [9] found with cats that oxalic acid poisoning strongly diminished the faradic excitability of the heart vagus, but the excitability of the pelvic

nerve, the chorda tympani and the cervical sympathetic was not diminished. On the other hand, certain chemical substances (pilocarpine, atropine, and adrenalin) acting at the periphery produce an increased action. These two effects—the diminished susceptibility of the nerve to faradization and the increased susceptibility to certain chemicals—are not antagonistic. Pilocarpine, adrenalin and atropine we know produce an increased action after section of the nerves to the tissues upon which they act, and if these nerves are allowed to degenerate the action is still further enhanced. This evidence tends to show, then, that the absence of calcium causes a block at the nerve-endings  $\gamma$ . In other words, the  $\gamma$  is paralysed, whilst the  $\beta$  is hyperactive to chemical stimuli. The nerve-endings are more susceptible to alterations in their calcium content than other parts of the nerve and other tissues. Absence of calcium, then, might be expected to antagonize the physostigmine action on nerve-endings ( $\gamma$ ) whilst enhancing the pilocarpine action (on  $\beta$ ). On the former point I have found no observations. The experiments of Ringer, Loeb, Meyer, and numerous other observers have demonstrated that an excess of calcium in the living tissues exerts a damping effect on all kinds of activity, especially on the vegetative nervous system, and a diminution of the permeability of the vessels. The experiments of Loewi and Ishizaka [57] have given these observers cause to believe that the diastolic standstill of the frog's heart in muscarine poisoning is due to the cessation of natural excitation, and that loss of calcium is either the sole or an important cause of the condition.

#### SELECTIVE ACTION ON OTHER FORMS OF PLAIN MUSCLE.

Many substances are known which have been regarded as exciting the "nerve-endings" to glands and plain muscle principally because their effect was annulled by the previous injection of atropine but not of nicotine; in these cases the end-organ was believed not to be affected by the atropine, since it responded to direct stimulation. Muscarine, pilocarpine, physostigmine, and colchicine are examples of such drugs. But there are many facts that tend to show that these drugs do not act upon the same substances or processes, and also that the peripheral autonomic nervous system, used in its widest sense, is not composed of chemically identical elements. Colchicine, for example, exerts the typical effect on "vagal endings" in the alimentary canal, but has little or no action on the iris, heart, or vessels; nor does it excite, except in the most trifling

manner, gland cells (Dixon and Malden [21]). Pilocarpine and physostigmine act differently upon plain muscle, and attention has already been drawn to this in the case of the heart and iris. Yet the action of all these substances is entirely annulled by a small injection of atropine, and the atropine was regarded as paralysing some peripheral structure—e.g., the “nerve-endings.”

But in some instances paralysis is not the explanation of the antagonism. Thus Bayliss and Starling [3] showed that while atropine antagonizes the effect of pilocarpine on the bowel as completely as on the heart and iris, it does not prevent the effect on the bowel of stimulation of the motor nerves, and Malden and I have shown the same to be true of the alkaloid colchicine. Some doubt has been expressed by Fröhlich and Loewi [27] on the validity of these experiments, but they have been confirmed by Cushny [12], who states that the violent movement of the intestine induced by pilocarpine may be antagonized by atropine without interruption of the path of the nerve impulse to the bowel. Nor is the bowel an isolated instance, for de Zilwa [91] found that muscarine caused a marked increase in the tonus of the retractor penis which was abolished by atropine, yet the muscle continued to contract on stimulation of its nerve. The violent contractions of the rabbit's uterus under pilocarpine are arrested by atropine, though stimulation of the hypogastric nerves continues to be effective (Cushny). Röhrig [75] and Langley and Anderson [51] had previously noted that atropine is devoid of effect upon the uterus and its motor nerve. Atropine removes the vaso-constriction produced by pilocarpine without paralysing the splanchnics [19], and Langley [49] has shown that the same facts hold for the bladder.

The antagonism between pilocarpine and apocodeine is in marked contrast with that between pilocarpine and atropine, because apocodeine in large doses paralyses only certain nerve-endings, and it is only in these cases that the action of pilocarpine is annulled. Thus apocodeine paralyses the sympathetic nerves to the intestine, but not those to the bladder, and pilocarpine and adrenalin are without effect on the former viscus, whilst producing their ordinary effect on the latter.

Before discussing how these effects are produced yet another paralysing drug, ergotoxin, requires attention, because arguments as to the seat of action of drugs are drawn occasionally from experiments in which this substance is used. Dale [17] showed that this alkaloid paralyses those structures which adrenalin stimulates. So that where the nerve supply from the sympathetic system is purely inhibitory ergotoxin is

without action either on the adrenalin effect or on sympathetic nerve stimulation (stomach, intestines, gall-bladder). If the sympathetic supply is purely motor the action of adrenalin or nerve stimulation is annulled (heart, dilator iridis, retractor penis, pilo-motor muscles, and ileo-colic sphincter). And last, if the sympathetic supply is mixed, ergotoxin removes the motor effects and leaves the inhibitory (the arteries of carnivora, spleen, uterus, &c.). Ergotoxin clearly, then, has a very specialized selective action on the motor elements of that structure, which is excited by adrenalin and by impulses in fibres of the true sympathetic system, the inhibitor elements being unaffected. Ergotoxin, like apocodeine, always acts, when it antagonizes the effect of an exciting drug, by paralysing the nerve.

Cushny [13] found that the motor effects of pilocarpine on the pregnant uterus are antagonized by ergotoxin injected previously, whilst the inhibitory action is unimpaired, and in this pilocarpine resembles adrenalin; but the pilocarpine effect is completely antagonized by atropine whilst the adrenalin action remains uninfluenced, and, further, not only is the motor action of pilocarpine abolished by atropine but its effects on the inhibitory functions also disappear. The relative degree of contraction or relaxation that pilocarpine produces on the uterus varies exactly with that produced by stimulation of the hypogastric nerves, so that it is difficult to avoid the conclusion that the alkaloid affects some point on the path of the nerve impulse. Cushny, however, is so impressed with the effect of atropine that he suggests a set of "receptors" for adrenalin and ergotoxin lying on the nerve impulse path, and a separate and independent "receptor" for atropine and pilocarpine associated with the impulse path but not on the direct course to the contractile substance. Nevertheless the "receptor" for atropine and pilocarpine in many other organs, such as the heart, iris, salivary glands, must lie on the nerve impulse path, for the antagonism of pilocarpine by atropine involves the interruption of this path.

Fröhlich and Loewi tabulated all the results of the action of atropine upon the effects of excitation of autonomic nerves, and came to the conclusion that it acted almost exclusively upon the augmentor fibres of the cranial and sacral autonomic system; they admit, however, one exception in the sweat-nerves. With our present knowledge it is almost impossible to place the action of these drugs (pilocarpine and atropine) under any general rule. Other obvious exceptions to the "rule" laid down by Fröhlich and Loewi are the paralysis of cardiac

inhibitory cranial nerves by atropine and its failure to paralyse cranial augmentor nerves (intestinal vagus) completely, though I believe there is some partial paresis. Atropine, then, paralyses most post-ganglionic cranial autonomic fibres, it readily paralyses the sympathetic sudoriferous fibres, and in larger amounts the sympathetic salivary fibres (cat). Then it passes to the sacral autonomic fibres and paralyses those which cause drawing down of the rectum.

It is easy by injecting physostigmine into the circulation of an animal to cause an apparent vagal paralysis, that is, a condition in which faradic excitation of the vagus is without action on the heart, and this at a time when the heart is beating well though slowly. I do not believe, however, that this paralysis is of the same nature as that induced by atropine, but rather that the peripheral vagal tissues are at a maximum degree of excitability, so that further stimulation either by electrical excitation of the vagus or injection of pilocarpine is without appreciable effect. One reason why I adopt this view is because a small injection of atropine into an animal showing such a paralysis at once causes a very decided acceleration of the heart with an increase in blood-pressure.

Degeneration of the post-ganglionic fibres to an organ does not interfere with the action of pilocarpine and atropine, indeed the action is rather more intense than otherwise. Fuchsinger believed that after section of the nerves to the cat's leg and allowing five or six days for degeneration, pilocarpine caused no sweating, but Langley and Anderson [52] showed that pilocarpine caused a secretion in the pads of the cat's feet six weeks after the removal of a portion of the sciatic nerve and before any regeneration had occurred. Brodie and Dixon [7] showed that pilocarpine retained its vaso-constrictor action on vessels at all periods up to three months after section of the vasomotor nerves; and numerous other examples occur in the literature which warrant the conclusion that in every case pilocarpine is at least as active after as before nerve degeneration.

#### ADRENALIN.

Lewandowsky [54] first made the suggestion that the action of suprarenal extract upon plain muscle corresponded with electrical stimulation of the sympathetic nerve supply to that particular muscle. Langley [50] also laid emphasis on this point and stated that the action evoked by the extract of suprarenals corresponded with stimulation of the



thoracico-lumbar or sympathetic set of the autonomic system. Brodie and Dixon gave a table showing that the action of adrenalin upon any tissue is invariably that which follows excitation of the sympathetic nerves supplying the tissue, and Elliott [25] gives a very complete summary of all the known actions. It is not necessary to describe in detail the action of suprarenal extract upon the different tissues of the body in various animals, and it is an accepted fact that the action of adrenalin takes place at the periphery and corresponds with the sympathetic stimulation. It can hardly be wondered at, then, that this fact alone came to be regarded as evidence that the adrenalin directly excited the sympathetic nerve-endings.

Much more recently the fact has been ascertained that the action of adrenalin is in proportion to the innervation of the viscus. Perhaps the clearest evidence of this is to be found in the blood-vessels of the body which respond very unequally to adrenalin, thus adrenalin causes great pallor of the uterus and but little in the bladder. In the abdominal viscera its effect is great on the main branches of the cœliac and superior mesenteric arteries whilst on the smaller branches of these arteries in the stomach and intestines it is less, whilst the veins in these organs are little if at all affected, and these effects correspond with the effects on sympathetic stimulation. No clear evidence exists that electrical stimulation of the sympathetic fibres coming off from the ganglion stellatum constrict the pulmonary vessels, and Brodie and Dixon have shown (*ibid.*) that perfusing these vessels with adrenalin causes no constriction in the dog, although Plumier [73] and Wiggers [89] through using enormous doses of adrenalin believed that trifling constriction did occur. The cerebral vessels also cannot be certainly affected by nerve stimulation, and Halliburton and Dixon [30] have shown that when isolated their perfusion with adrenalin is without a constrictor effect, although Wiggers, by perfusing in situ believes that the slight constriction which he saw was due to an action on these vessels. *It may, then, be accepted that the degree of innervation and the effect of adrenalin go hand in hand.*

One further proof that the action of adrenalin is in some way associated with the sympathetic nerves may be obtained by paralysing the vaso-constrictor fibres with apocodeine, when it is found that adrenalin has either lost its action or induces vaso-dilatation. Nevertheless, the contractile substance of the arterioles must be intact, since the muscle responds in the normal way to muscle poisons.

Ergotoxin has a still more selective action than adrenalin, since



it paralyses only the peripheral *motor* elements, which are excited by adrenalin and by impulses in the fibres of the true sympathetic system, the inhibitory elements being unaffected. The effect of this drug can be seen at a glance from the following table:—

| Origin                                    | Effect of exciting the sympathetic or<br>injecting adrenalin |                    |
|---|--|--------------------|
|   | Before<br>ergotoxin  | After<br>ergotoxin |
| Arterioles ... ..                         | M  | I                  |
| Heart ... ..                              | M  | —                  |
| Spleen ... ..                             | M  | I                  |
| Ileo-colic sphincter ... ..               | M  | —                  |
| Internal anal sphincter ... ..            | M  | I                  |
| Fundus of urinary bladder (ferret) ... .. | M  | I                  |
| Base of bladder and urethra ... ..        | M  | —                  |
| Pilo-motor muscles ... ..                 | M  | —                  |
| Dilator iridis ... ..                     | M  | —                  |
| Uterus (non-pregnant) ... ..              | M or I   | I                  |
| Uterus (pregnant) ... ..                  | M  | I                  |
| Retractor penis ... ..                    | M  | —                  |
| Stomach ... ..                            | I  | I                  |
| Small intestine ... ..                    | I  | I                  |
| Large intestine ... ..                    | I  | I                  |
| Gall-bladder ... ..                       | I  | I                  |
| Fundus, urinary bladder (cat) ... ..      | I  | I                  |

M = motor effect—i.e., increase of tone or augmentation.

I = inhibition—i.e., relaxation of tone or weakening.

All this evidence, whilst it clearly associates the sympathetic system with adrenalin, in no way helps us in localizing the seat of action at the periphery. Elliott (*ibid.*, p. 429) showed that adrenalin had no effect on the cells of the peripheral visceral ganglia nor on the peripheral nerve-trunks. Several observers have adopted the method of degeneration with a view to determining the seat of action, and their results are in accordance—namely, that degenerative section of the sympathetic nerves does not hinder the action of adrenalin, so that Lewandowsky [55] and Langley were inclined to refer the excitation to the plain muscle cells.

Lewandowsky shows that suprarenal extract had its usual action on the eye three weeks after extirpation of the superior cervical ganglion, and his observations were confirmed by Langley. Meltzer and ~~Meltzer~~ Auer [65] excised the superior cervical ganglion, and after allowing time for degeneration found that adrenalin was more active than before. Elliott removed both the superior cervical ganglion and the ciliary, and obtained like results—that is, increased sensitiveness to

adrenalin. He also performed experiments with the retractor penis of the dog and the bladder of the cat, and after denervation found that adrenalin acted at least as well as before. These experiments were not, however, so satisfactory in regard to certainty of complete denervation as those on the iris of the cat. Brodie and Dixon showed that after section of the nerves to the cat's hind limb and allowing a variable time, from four days to three months, for degeneration, that the blood-vessels constricted at least as well to adrenalin as in the normal limb, and Meltzer showed that the denervated muscles of the rabbit's ear become more sensitive to adrenalin. Langley's experiments, in which he excised the superior cervical ganglion, also proved that the hair muscles are in agreement with other muscles in exhibiting greater irritability towards adrenalin when denervated.

It is quite clear, then, that adrenalin cannot act on the nerve-endings in the ordinary sense, that is, the terminal fibres as revealed by methylene blue. A few experiments have been made by Fletcher on the nerve plexus in the retractor penis of the hedgehog. In these he found that the nerve plexus did not stain with methylene blue after degenerative section of the nerves supplying the muscle. The argument so far is based on the assumption that the nerve-fibres on section degenerate up to the peripheral plexus.

Adrenalin certainly does not act on the contractile substance. The proofs in this case seem overwhelming. First, as already pointed out, we can antagonize the effects of adrenalin, either the motor only (ergotoxin), or the whole effect (apocodeine), leaving the response of the muscle to mechanical or chemical stimuli intact. Secondly, the established fact that the response of plain muscle to adrenalin is determined by the presence of a sympathetic nerve supply. One example will make this point clear. The bladder of the cat has motor fibres from the sacral, and inhibitory from the sympathetic, and the inhibitory fibres are a specific development in the cat. Elliott in his numerous experiments on the cat's bladder found two abnormal cases, in which excitation of the hypogastric nerves failed to inhibit the bladder whilst affecting the urethra and vesiculæ seminales normally. In each of these two cases adrenalin could neither inhibit the bladder nor lessen the contraction caused by stimulation of the pelvic visceral nerves: dissection in these cases showed that the hypogastrics did not supply the usual fibres to the vesical plexus. The bladder of the ferret contracts under normal conditions when either the sympathetic or the sacral nerves are stimulated or when adrenalin is given. After ergotoxin, stimulation of

the sympathetic nerves or the administration of adrenalin causes inhibition, yet the contractile substance must be normal, since stimulation of the sacral nerves produces much the same effect as before. Thirdly, it is not easy to appreciate how the blood-vessels of the lungs, heart, and brain should differ in their musculature from those of the limb or intestine to such an extent that whilst the latter group are intensely affected by adrenalin, the former are either not influenced or only in the most trifling degree. Fourthly, the special relationship of adrenalin to sympathetic nerves is strongly supported by the fact of the close developmental connexion of the suprarenal bodies with the sympathetic ganglia.

To meet these requirements Brodie and Dixon extended the word "nerve-ending" to mean the connecting link between nerve-fibre and muscle-fibre, which they term the neuro-muscular tissue; Elliott adopts the term "myo-neural junction" and Langley "receptive substances." The question so far, then, is largely a matter of nomenclature, and the only legitimate statement from the premises is that adrenalin does not act on contractile substance nor on nerve substance outside the limits of the myo-neural junction. Elliott considers that the substance which is stimulated by adrenalin is not an intrinsic part of the muscle, but is developed from the muscle in consequence of its union with a sympathetic fibre, in which case, of course, it cannot develop in the embryo until after the sympathetic nerves are functional. Observations on the time at which poisons begin to take effect on the embryo have failed to throw light on the question.

All other substances except adrenalin evoke from the group of plain muscle tissues, when stimulating them directly, a reaction differing only in degree and not in kind in each tissue. It is the peculiarity of adrenalin to cause sharp contraction in the one and relaxation in the other. The cause is the same: the effects differ. Therefore the reacting substances must be different. And since other mechanical and chemical stimuli do not point to marked intrinsic differences in the plain muscle-fibres, whereas they do reveal differences in the "nerve-endings," we must regard the difference at present as inherent in the "myo-neural junction."

#### SYMPATHO-MIMETIC SUBSTANCES.

The elucidation of the structure of adrenalin and its synthesis by Stolz [82] and by Dakin [15] naturally led to the investigation of allied substances. Loewi and Meyer [58] investigated a series

of ketones of the general formula  $(\text{OH})_2\text{C}_6\text{H}_3\cdot\text{CO}\cdot\text{CH}_2\text{NR}_1\text{R}_2$  and their corresponding secondary alcohols. Dakin confirmed the results of Loewi and Meyer. Barger and Dale [2] adopt the term "sympatho-mimetic" to represent an action of a drug which simulates stimulation of the sympathetic nervous system: they state that all the substances producing this action in characteristic manner are primary and secondary amines, and that the quaternary amines have an action similar to that of nicotine. The optimum carbon-skeleton for sympatho-mimetic activity consists of a benzene ring with a side-chain of two carbon atoms, the terminal one bearing the amino group. Another optimum condition is the presence of two phenolic OH groups in the 3:4 position relative to the side-chain (Harold Nierenstein and Roaf).

A very large number of substances are now known which exhibit this sympatho-mimetic action. The primary amines—butylamine, amylamine, hexylamine—show the effect in a more or less typical manner; in the higher members of the series this effect is complicated by a depressant action on muscle. The aromatic amines which do not possess a phenolic (OH) also exhibit this effect; to produce an optimum action the side-chain of the ring should carry two carbon atoms, of which the second bears the amino group. Of the amines containing one phenolic (OH), the best known is *p*-hydroxyphenylethylamine, which is a pressor constituent in putrefying meat and in ergot.<sup>1</sup> The relative action of the amines with two phenolic hydroxyls on the blood-pressure is roughly as tabulated below:—

|  |     |     |     |      |
|--|-----|-----|-----|------|
| $(\text{OH})_2\text{C}_6\text{H}_3\text{COCH}_2\text{NH}_2$ ...                                  | ... | ... | ... | 1.5  |
| $(\text{OH})_2\text{C}_6\text{H}_3\text{COCH}_2\text{NH}\cdot\text{C}_2\text{H}_5$ ...           | ... | ... | ... | 2.25 |
| $(\text{OH})_2\text{C}_6\text{H}_3\text{COCH}_2\text{NH}\cdot\text{C}_6\text{H}_7$ ...           | ... | ... | ... | 0.25 |
| $(\text{OH})_2\text{C}_6\text{H}_3\text{CH}_2\text{CH}_2\text{NH}_2$ ...                         | ... | ... | ... | 1.0  |
| $(\text{OH})_2\text{C}_6\text{H}_3\text{CH}_2\text{CH}_2\text{NH}\cdot\text{CH}_3$ ...           | ... | ... | ... | 5.0  |
| $(\text{OH})_2\text{C}_6\text{H}_3\text{CH}_2\text{CH}_2\text{NH}\cdot\text{C}_2\text{H}_5$ ...  | ... | ... | ... | 1.5  |
| $(\text{OH})_2\text{C}_6\text{H}_3\text{CH}_2\text{CH}_2\text{NH}\cdot\text{C}_6\text{H}_7$ ...  | ... | ... | ... | 0.25 |
| $r(\text{OH})_2\text{C}_6\text{H}_3\text{CH}(\text{OH})\text{CH}_2\text{NH}_2$ ...               | ... | ... | ... | 50   |
| $r(\text{OH})_2\text{C}_6\text{H}_3\text{CH}(\text{OH})\text{CH}_2\text{NH}\cdot\text{CH}_3$ ... | ... | ... | ... | 35   |

One other fact may be of significance here—the stereo-isomeric condition of the compound. Cushny has shown that adrenalin acts approximately twice as strongly in stimulating the sympathetic system as racemic adrenalin, an analogous observation to what has been observed in the activities of other stereo-isomerides, such as the

<sup>1</sup> Barger and Walpole, *Journ. of Physiol.*, 1909, xxxviii, p. 343; Dale and Dixon, *ibid.*, 1909, xxxix, p. 25.

nicotines and hyoscyamines. In a general way it may be stated that approximation to adrenalin in structure is attended by increase of sympatho-mimetic activity.

The most striking feature in the action of these bases is the more or less strict localization of their action to cells innervated by the sympathetic system. Barger and Dale think it possible that the stimulant activity may depend on one property and the distribution of the action on a different property. This possibility may of course be true, but if so it is certainly not in accord with the distribution of specific alkaloids. Nicotine, which is perhaps most nearly allied to the bodies under consideration, does not seem to be attracted especially to the tissues upon which it acts, but tends to collect in the liver. The only complex common to all these bases is the group  $\text{C}-\text{C}-\text{N}$ , and this, of course, is present in innumerable bases having no sympatho-mimetic activity. So soon as we attempt to apply the side-chain hypothesis to the action of drugs we are attacking the old problem of the relation of chemical constitution to physiological action. The side-chain hypothesis necessitates an indefinite number of these side-chains for each new base with sympatho-mimetic properties.

#### CONCLUSIONS.

In conclusion, I will very briefly review the various hypotheses which have been suggested to account for specificity of drugs on peripheral end-organs. The permeability of the cell, the solvent power of its limiting layer, and surface tension have each been suggested as possible explanations.

Straub [83] suggests that inhibition of the heart by muscarine is caused by the physical process of the passage of muscarine through the limiting layer of the cell, and that when it has passed this layer it cannot cause inhibition. He finds that in *Aplysia* muscarine is stored in the heart muscle, and that a certain amount in the outside fluid is necessary for inhibition. If this surrounding fluid is removed, the inhibition is removed. He found, further, in the Selachian heart that atropine delayed the absorption of muscarine, and suggests that atropine in some way alters the limiting membrane, so as to retard the absorption of muscarine below the threshold velocity necessary to produce an action. Cushny argues that Straub's view may be consistent with the fact that atropine antagonizes pilocarpine in the uterus without interfering with the passage of the nerve impulse, but on the other

hand it fails to explain its simultaneous antagonism to pilocarpine and interference with the passage of the impulse in other organs such as the heart. Langley also argues that it cannot explain the antagonism between curare and nicotine on the sartorius of the frog. Straub finds, however, that this law does not necessarily hold in all cases, as, for example, the frog's heart, since muscarine may produce inhibition at a time when absorption must have ceased. But even supposing that a drug only acts in the course of its permeation into the cell due to a concentration difference inside and outside, this does not explain why strychnine, which he finds is absorbed, does not cause inhibition. In other words, whilst physical factors, as probably all are ready to admit, may be of the greatest importance in limiting the action of a drug, they cannot be accredited with determining the specific type of action. It is difficult, for example, to explain on this hypothesis why adrenalin may cause either inhibition or contraction within the same class of tissue cells, or why a nerve becomes paralysed as a result of giving a stimulating poison.

The knowledge that certain substances are refused admission into cells has long been recognized. Magnesium sulphate cannot penetrate the cells of the alimentary canal; tetanus toxin and probably the alkaloid colchicine cannot penetrate the membrane of the nerve cells, and absorption into them can only take place through the nerve-endings; ammonium chloride, on the contrary, penetrates almost all cells with the greatest ease, the rate of penetration being out of all proportion to any osmotic changes which may be present. It has, naturally enough, then, been suggested that the specific affinity of a drug for a nerve-tissue may depend first upon its partition co-efficient, and secondly on some chemical action after absorption. Thus the hypotheses of Traube and Overton-Meyer can account for the specific selective action of the central nervous system for the indifferent hypnotics, whilst the hypothesis of Baglioni explains a possible mode of action after entrance to the cell has been obtained. Barger and Dale also suggest that this double factor may come into play in the case of the sympatho-mimetic amines, but as they point out, this supposition is supported by no positive facts. Without entering into this question, I believe one may take the broad view that drugs exerting a selective action on one or more tissues in relatively small doses (0.1 gm. or less in the case of man) do not tend to collect in the cells upon which they act more than in other cells; indeed, the reverse may be the case.

Before considering the purely chemical hypothesis I will refer again

to the results of Lucas on voluntary muscle, in which he clearly showed the existence of three excitable things, one associated with the nerve, one with the muscle, and the most highly excitable, the  $\beta$ , neither associated with the ordinary muscle nor yet with the nerve, but localized in the region of the nerve-ending. If it is legitimate to extend this conception to plain muscle, we obtain an explanation of most of the phenomena with which we have been dealing. Atropine should then be regarded as removing the excitability of the  $\beta$  so that the nerve impulse can no longer reach the  $a$ . Pilocarpine also affects the  $\beta$ .

Sometimes, however, as in the bladder, atropine may still eliminate the pilocarpine action without paralysing the nerve, though it weakens its effect. In this case it is obvious that only a portion of the highly excitable  $\beta$  is paralysed (*see* fig. 1). Supposing that pilocarpine and

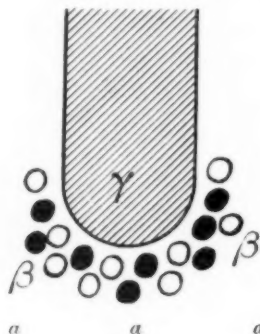


FIG. 1.

atropine act upon the clear rings, then after a dose of atropine pilocarpine can no longer produce an effect, though  $\gamma$  can still communicate with the  $a$  by the unparalysed portion of the  $\beta$ . If this diagram represents the nerve-endings in the uterus we can conceive adrenalin as acting on the  $\beta$  dark circles with undiminished activity, since these are not influenced by atropine, whilst ergotoxin would completely paralyse all the  $\beta$  whilst leaving the  $a$  intact, since we know that the contractile substance has lost little or none of its excitability to direct stimulation.

It is quite conceivable, however, that the nerve to the bladder, uterus and intestine is a mixed nerve, just as we know the sympathetic may be a mixed nerve, in which case the diagram would be more correctly shown in fig. 2. This diagram might also be used to explain the



condition in a mixed motor inhibitory sympathetic nerve. Adrenalin in this case causes an explosion in the  $\beta$ , and induces a mixed augmentor inhibitory effect. It is difficult to understand how it comes about that two nerves of essentially the same nature should attract to the neighbourhood of the endings substances of different excitabilities; or it may be that the reverse is true, and that the highly excitable  $\beta$  determines in some tactic way the position of the ultimate nerve-endings, and in support of this is the fact that the  $\beta$  retains its excitability even in an exaggerated degree months after degenerative section of the nerve.

The chemical hypotheses must, in the absence of any definite evidence of chemical combination, necessarily be highly speculative. Langley thinks that there is nothing in the nerve muscle preparation which can, with any plausibility, be taken as a structure not forming a

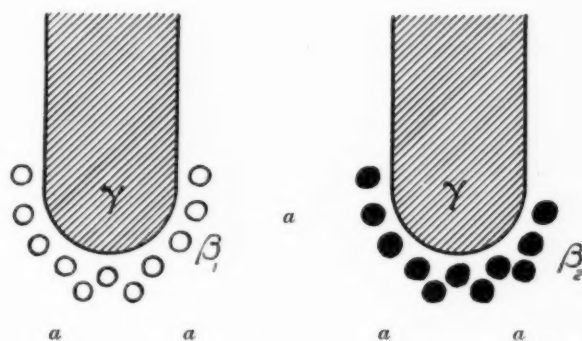


FIG. 2.

part either of the nerve or muscle (contractile substance). He regards the contractile molecule as carrying receptive or side-chain radicles with which drugs may combine; thus nicotine by combining with one causes tonic contraction and with another twitching, and he thinks that in no case have chemical substances a special action on nerve-endings. I have had occasion, earlier in this address, to mention Langley's explanation of the experiments of Anderson, Magnus and Fühner, all of which appear to oppose directly this supposition. Hill's mathematical investigation of the contraction curve of frog's muscle in response to nicotine under varying conditions leads him to the conclusion that the act of stimulation depends on a chemical reaction, and whilst most of us are probably willing to accept this as proven, it affords no evidence that nicotine undergoes any chemical change.

The earlier views of Dixon and Hamill [20] are that activity in a tissue can only be produced in one way, and that drugs act by liberating a specific hormone, which combines with some constituent in the end-organ, and further that nerve stimulation induces activity in just this same manner. Criticisms of this view have been made by Langley, and Barger and Dale.

My present attitude leads me to lay stress on the experimental proof that Lucas has given of the three excitable things in voluntary muscle of the frog. It seems to afford a working hypothesis built on fact, which will account for most if not all the phenomena and paradoxes of drug action. The neuro-muscular junction of Brodie and Dixon, the myoneuronal junction of Elliott, are represented by the  $\beta$ . This view also suggests that normal functional activity and drug actions may be produced in the same way by an explosion of the  $\beta$ ; so that whether the excitability of the  $\beta$  is raised through  $\gamma$  or by a drug directly, it affects the  $\alpha$  in the same way in each case.

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SIR LAUDER BRUNTON, F.R.S., said he was sure all present had listened with intense pleasure to the address of their President. Professor Dixon had handled his subject with extreme care, and had chosen one of the most difficult subjects in pharmacology. Amongst workers in this line there had been as many differences of opinion as there were workers and experimenters, and Dr. Dixon had placed all the views before the meeting in this paper very carefully and thoroughly. Perhaps he had said less than one would have wished about "chemo-ceptors," bearing in mind that this was a very interesting matter at the present moment in view of the introduction by Ehrlich of salvarsan, which had been really introduced in this way. It was well known that when one's hands became greasy, and were placed into water, the grease would not come off. But if a little potash was put on it would form a chemo-ceptor with the grease and the hands could be cleaned. In the same way with spirochaetes and arsenic; spirochaetes would be poisoned by arsenic, but arsenic would not attack them unless a chemo-ceptor were present to make it do so. Ehrlich found one among the benzene group which had this effect, and so salvarsan was introduced. It would be difficult to say what the chemo-ceptor was in the nerve-endings. He had been much interested in the last expression used by the President in "the explosion of the Beta substance," because in some experiments which he made many years ago with ammonium compounds he found that when the muscle was poisoned with some of the ammonia salts the first stimulation of a nerve would cause the muscle to contract, like normal muscle, but after that it seemed as if the first impulse had exploded the connexion between the nerve and the muscle, and it would not react, although the muscle itself would react. He hoped the address would be published in full before long, because it contained an immense amount of information—more than he had ever seen collected on the subject before, and he thought it would be a long time before such a mass would be collected again. One wished to study not only the general points which the President had brought forward, but those very particular ones which time did not permit him to deal with.

## Therapeutical and Pharmacological Section.

November 19, 1912.

Professor A. R. CUSHNY, F.R.S., Vice-President of the Section,  
in the Chair.

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### The Action of Pilocarpine and of Atropine on the Urinary Secretion.

By DOUGLAS COW, M.D.

MANY and divergent results have been obtained by various investigators working on the action of these drugs on the urinary apparatus. Thus Spiro and Vogt [13] state that pilocarpine has no definite action on urine secretion, and that after atropine pilocarpine produces no change. Schmiedeberg [12] considers that pilocarpine has no direct action on the flow of urine; and Cushny [3] states that the flow of urine is unaffected by pilocarpine, excepting that loss of fluid by other glands causes an indirect diminution. On the other hand, René [11], working with the kidney oncometer, finds that pilocarpine produces an increase in kidney volume, with a concomitant increase in the flow of urine. Walti [16] and Thompson [15] conclude that diuresis is diminished or interrupted by atropine, though the blood-pressure is at the same time slightly raised. Lazzaro and Pitini [7] found that in dogs pilocarpine produces a diminution in the flow of urine. Maccallum [9] states that when diuresis is copious minute quantities of pilocarpine produce a distinct diminution in the amount of urine excreted, and that the subsequent injection of atropine neutralizes this pilocarpine effect. He states, too, that atropine sometimes has no effect on the flow of urine, and sometimes diminishes the flow; and that when the flow is thus diminished the subsequent injection of pilocarpine neutralizes the atropine effect. This author endeavours to explain these actions by suggesting that atropine may act on the convoluted tubules, which are

similar in structure to glands on which atropine has a definite action; and that pilocarpine acts on the muscular tissue in the walls of the renal artery and on possibly existing smooth muscle-fibres in the substance of the kidney itself.

#### METHOD.

Dogs were the animals used. In my earlier experiments the animals were provided with permanent bladder cannulæ to which stop-cocks were attached. These cannulæ were inserted by means of purse-string sutures and under strict asepsis. A week to ten days was allowed for the animals to recover from the effects of the operations, after which time it was found that they stood manipulations of the stop-cock without discomfort. The advantages of this method of studying conditions of urinary secretion are pointed out by Ginsberg [5]. The animals were placed on a fixed diet of moist, uncooked tripe, 500 grm. of which were allowed for a dog of 7.5 to 8 kilos, given once a day; no water was allowed.

During the actual experiments the animals were attached to a long chain, so that they could (within limits) move about freely. At the commencement of each experiment the urine was drawn off and a known quantity (generally 2 c.c.) of saline injected through the cannula, and immediately withdrawn and measured, to ensure that there was no fluid left in the bladder, and that there was no stoppage in the cannula. Thereafter the urine was drawn off at regular intervals (sometimes every five minutes, sometimes every ten minutes) and accurately weighed, so that any slight variation in the amount excreted at once became apparent. On the fixed diet and under normal conditions this five- or ten-minute excretion was found to remain very constant, about 1.3 c.c. being excreted every ten minutes. It should be stated that the daily meal was given about 8 p.m., so that the temporary increase in diuresis caused thereby had passed off by the next morning, and from 9 a.m. until after the next meal at 8 p.m. the normal flow was found to remain very constantly at about the above figure.

It was found that 50 c.c. or 100 c.c. of water given *per os* produced a regular increase in diuresis, with its point of maximum intensity occurring about fifty minutes after the water was given, but that if 2 mgrm. of atropine were injected subcutaneously at the same time that the water was given, the maximum increase in diuresis did not occur until one hundred and ten minutes after the water was given. The total amount of fluid excreted was not diminished. When pilocarpine

(2 mgrm.) was given in the same way there was no appreciable delay in the excretion, but less was excreted than with water only.

An attempt was then made to isolate the ureter on one side from the action of the drugs as follows: On different occasions four dogs were anaesthetized with urethane, the abdomen was opened, the bladder drawn forward, and the left ureter isolated and ligatured near its junction with the bladder. This ureter was then opened on the proximal side of the ligature, and a flexible metal cannula was introduced and pushed up so that its end reached well into the hilus of the left kidney; the cannula was then firmly tied in this position. A puncture was then made in the bladder and a cannula tied in with a purse-string suture. It was hoped that in this way some difference in the secretion of the two kidneys might be manifested after the exhibition of pilocarpine or of atropine. In one experiment, indeed, some slight difference was noted after the injection of pilocarpine, but though all precautions were taken to combat shock from the operation the flow of urine was so small in amount that any differences were too small to be reliable. In one of these experiments an attempt was made to increase the secretion of urine by giving water, but though 500 c.c. were given no increase in the amount of urine took place for five hours. Two dogs were then operated on in a similar way under ether and morphia, and with strict aseptic precautions. Two days after the operations, when the effect of the morphia had worn off, they were ready for experiment.

We had then two dogs, in each of which the urine from the left kidney flowed away directly through a metal cannula, so that no constriction or dilatation of the ureter could influence it in any way, and in which the urine from the right kidney passed through the ureter and bladder, and so out through a bladder cannula. These animals had recovered from operation shock, and were not under the influence of any anaesthetic. During the experiments these animals were slung up in slings, and the urine from the two kidneys was collected separately in tared flasks and accurately weighed at intervals of either five or ten minutes.

At the commencement of each experiment 100 c.c. of water were given *per os*, in order to increase the amount of urine secreted, so that any difference that might occur between the two sides should be as marked as possible. When water only was given it was found that the flow from the two kidneys ran in absolutely parallel lines (Chart I), though the amount excreted by the left kidney was in neither case quite so much as that coming from the right kidney. Allard [1] has shown



that the secretion of urine from the two kidneys is parallel, though normally there may be a variation of as much as 30 to 40 per cent. in the amount voided by each, when much urine is being secreted. Possibly, too, the necessarily greater amount of manipulation undergone by the left kidney in these animals may have caused them to be slightly less effective than their fellows.

In these experiments the pilocarpine and atropine were given subcutaneously shortly before the height of the diuresis, caused by the water ingested, was reached; generally about forty-five minutes after the water was given. It was found in every case that atropine prolonged

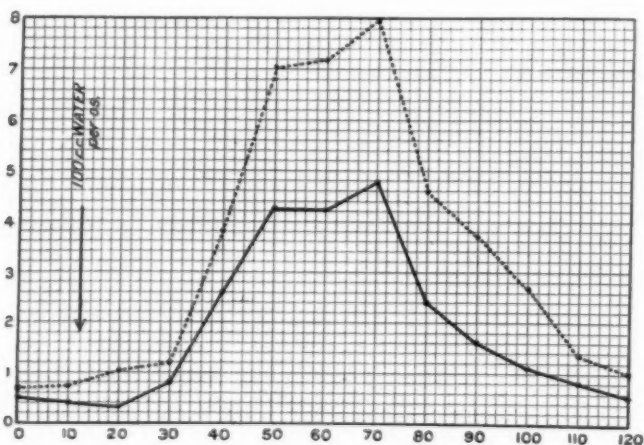


CHART I.

— Flow from left kidney (cannula in pelvis).

..... Flow from right kidney (via ureter and bladder).

Ordinate = Urine in cubic centimetres. Abscissa = Time in minutes.

the increase in diuresis from the right kidney (from which the urine flowed via ureter and bladder), whilst the flow from the left kidney (cannula in pelvis) followed a perfectly normal course, as if no drug had been given. The maximum increase occurred ten minutes later in the case of the right kidney than in that of the left, and the return to the normal level was still further delayed. Also in every case thirty to forty minutes after the maximum increase and forty-five to fifty-five minutes after the injection of atropine a more or less distinct further increase was noticed in the flow from the right kidney only (Chart II).

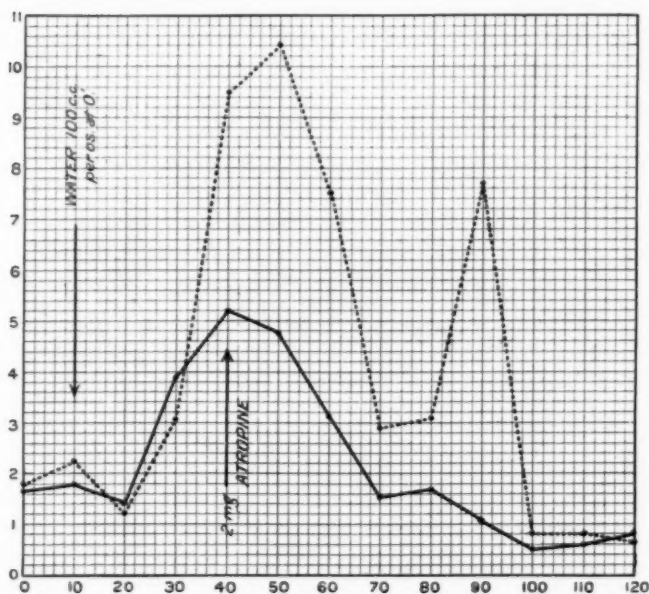


CHART II.

— Flow from left kidney (cannula in pelvis).  
 ..... Flow from right kidney (via ureter and bladder).

Ordinate = Urine in cubic centimetres. Abscissa = Time in minutes.

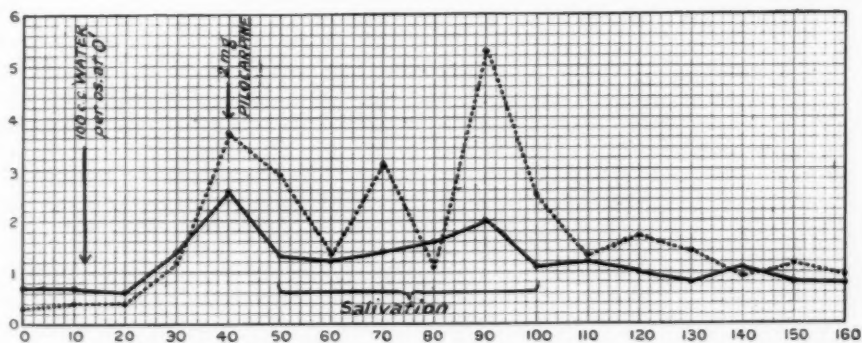
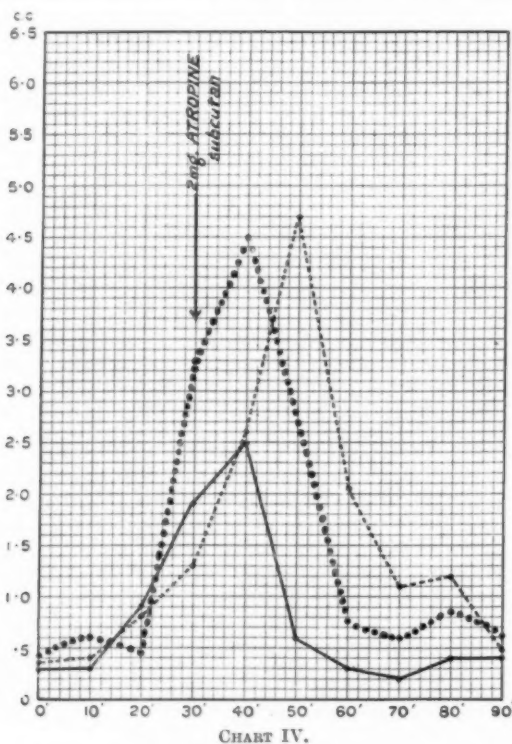


CHART III.

— Flow from left kidney (cannula in pelvis).  
 ..... Flow from right kidney (via ureter and bladder).

Ordinate = Urine in cubic centimetres. Abscissa = Time in minutes.

When pilocarpine was given it was found that the flow of urine from both kidneys was altered. Immediately following the injection of this drug came a sudden diminution in the amount flowing from both kidneys, followed in the case of the left kidney (cannula in pelvis) by a gradual rise of smaller or greater extent. The flow from the right kidney, on the other hand, underwent several further almost rhythmical alternations of increase and diminution, one of which secondary increases



- CHART IV.
- ..... Normal output of urine from both kidneys, 50 c.c. water *per os* at 0'. No atropine.
  - Flow from left kidney with cannula in pelvis, 100 c.c. water at 0'. Atropine at 30'.
  - - - - - Flow from right kidney (via ureter and bladder), 100 c.c. water at 0'. Atropine at 30'.

always exceeded the height of the original rise, which had been interrupted by the pilocarpine. The total amount of urine secreted in any given time after pilocarpine was less than with water only (Chart III). Charts IV and V show the effects of water only, and of water and

atropine, and water only, and water and pilocarpine, the curves being taken from the figures given by actual experiments and superimposed strictly to scale, in order to contrast these effects.

The total amounts of urine excreted by the two kidneys in a given time after these drugs, contrasted with the amounts voided by them

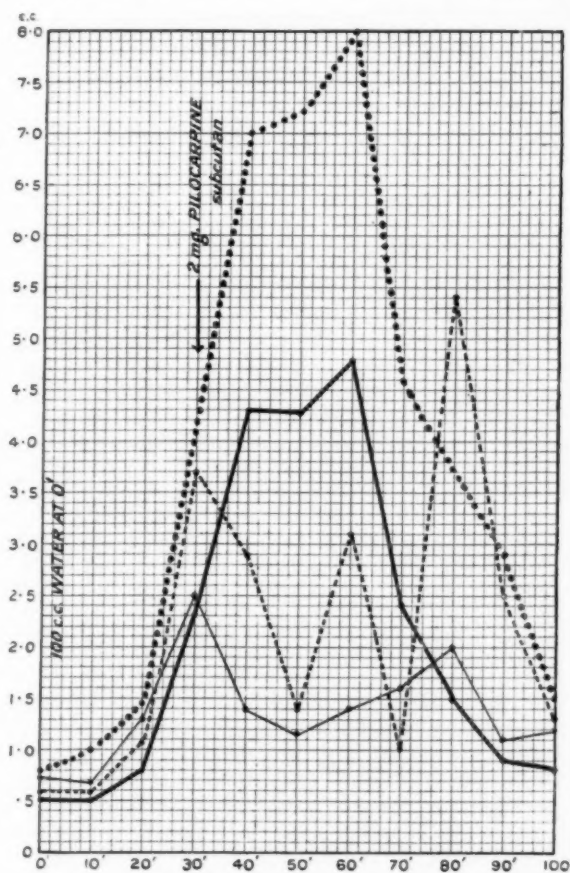


CHART V.

- |       |  |                          |
|-------|--|--------------------------|
| ..... | Output of urine from right kidney (via ureter)       | } Water only.            |
| —     | Output of urine from left kidney (cannula in pelvis) |                          |
| ----  | Output of urine from right kidney (via ureter)       | } Water and pilocarpine. |
| —     | Output of urine from left kidney (cannula in pelvis) |                          |

Ordinate = Urine in cubic centimetres. Abscissa = Time in minutes.

before the drugs were injected, furnish striking results. These are best given in tabular form :—

|              |     |     |     | Before atropine<br>c.c.    |     | After atropine<br>c.c.    |     |
|--------------|-----|-----|-----|----------------------------|-----|---------------------------|-----|
| Right kidney | ... | ... | ... | 17.37                      | ... | 31.88                     | ... |
| Left "       | ... | ... | ... | 15.51                      | ... | 13.86                     | ... |
| Right "      | ... | ... | ... | 18.40                      | ... | 34.77                     | ... |
| Left "       | ... | ... | ... | 13.93                      | ... | 15.08                     | ... |
| Right "      | ... | ... | ... | 7.33                       | ... | 23.89                     | ... |
| Left "       | ... | ... | ... | 7.04                       | ... | 8.83                      | ... |
| Right "      | ... | ... | ... | 23.55                      | ... | 37.40                     | ... |
| Left "       | ... | ... | ... | 21.54                      | ... | 20.93                     | ... |
|              |     |     |     | Before pilocarpine<br>c.c. |     | After pilocarpine<br>c.c. |     |
| Right kidney | ... | ... | ... | 9.57                       | ... | 42.06                     | ... |
| Left "       | ... | ... | ... | 7.45                       | ... | 22.74                     | ... |
| Right "      | ... | ... | ... | 7.39                       | ... | 23.66                     | ... |
| Left "       | ... | ... | ... | 6.85                       | ... | 14.15                     | ... |

These results show that atropine, whilst it has no appreciable effect on the flow passing through the ureteral cannula on the one side, has a distinct effect on the flow through the normal ureter on the other side. To explain these phenomena I would suggest that a certain normal tonus in the ureters offers a resistance to the passage of urine; that this tonus, as would be expected, is relaxed by the atropine, and in consequence a more generous and prolonged outflow of urine takes place. Moreover, the secondary rise, which is in no case comparable to the first in magnitude, can then be explained by the passing off of the atropine effect, with consequent return of tonus to the ureter, which forces out the urine then contained therein.

The following theory appears to meet the case of the action of pilocarpine: The primary fall in the excretion of both kidneys is contemporaneous with the onset of salivation, lachrymation, and presumably of secretion from other glands; "the heart-beat is at the same time slowed from peripheral vagus stimulation and the blood-pressure falls" (Dixon [4]), so that diminished blood-pressure and loss of fluid by other glands can quite easily account for this primary fall. The next phenomenon is a sudden rise in the urinary outflow from the right kidney (via ureter and bladder), whilst that from the left kidney remains low. The cause of this must obviously be sought for in some influence affecting the urinary apparatus on the right side and not on the left. If we imagine, and it does not appear improbable, that at the time that

salivation commences the ureter becomes thrown into strong contractions by the pilocarpine, we have an additional cause for the primary fall in the output of urine from the right kidney (and, as a matter of fact, it is in all cases more marked on this side); thus a strong resistance would be offered to the outflow of urine on the right side, but after a time the pressure of the urine secreted by this kidney would overcome this resistance, resulting in a sudden outgush of urine, which is represented in these curves by the secondary rises in the output of the right kidney. The more gradual secondary rise in the output of the left kidney takes place contemporaneously with the falling-off of salivation, lachrymation, &c.; in other words, the effect of the pilocarpine is gradually wearing off, and the conditions are returning to the normal.

Confirmation of this theory was afforded by one of my earlier experiments conducted under urethane, in which, after the exhibition of pilocarpine, the flow from the right kidney (via ureter and bladder) was seen distinctly to come in a regular, rhythmical manner—three to five drops flowing in quick succession, followed by a pause during which no urine escaped until the next series of rapidly flowing drops. This phenomenon lasted for twenty minutes, and started almost immediately after the pilocarpine was injected.

Lewin and Goldschmidt [8] have shown that reabsorption can take place from the ureters. This may perhaps help to explain the fact that rather less urine is excreted after pilocarpine than normally, for during the periods of strong contraction of the ureters the urine is being held back and some reabsorption may take place.

Styrer [14] demonstrated that compression of the ureters causes a distinct increase in the amount of urine excreted, and this fact may account in some way for the markedly larger quantity of urine excreted by the right kidney than by the left in these experiments with pilocarpine, and it may also explain why, in every case after pilocarpine, one of the secondary rises in the output from the right kidney exceeds the primary rise in extent.

Metzner [10], too, states that the normal ureteral peristalsis may be influenced by various means, and that an anti-peristalsis can also take place.

Langley and Anderson [6] have clearly demonstrated the sympathetic nervous connexions of the ureters and adjacent viscera. These organs, however, in common with others as far as anatomical research goes, would appear to be without pelvic nerve supply. It is, however, well known that different kinds of stimulation will produce two

distinct varieties of salivary secretion, and that in the case of the bronchioles there are both constrictor and dilator fibres, as shown by Brodie and Dixon [2]. So that it is perhaps not an unlikely supposition that also in the innervation of the ureters there are similar nerve-fibres, whether contained in the hypogastric nerve or not, on whose nerve-endings in the ureters atropine and pilocarpine can act in their customary manner.

#### CONCLUSIONS.

(1) That the chief action of atropine on the excretion of urine is one on the plain musculature of the ureters.

(2) That pilocarpine affects the output of urine both indirectly through loss of fluid from other glands and also, and probably to a greater extent, by its action on the musculature of the ureters.

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### On the Action of a Tissue Extract in the Production of Diuresis.

By DOUGLAS COW, M.D.

GINSBERG [2] has shown that if varying quantities of water are given by mouth to dogs the resulting increase in diuresis is approximately proportional to the amount of fluid imbibed; also that if the same quantities of water are injected subcutaneously no increase in diuresis takes place. I have repeated these experiments, employing the method described by him, and my results agree with those of Ginsberg in all respects, excepting that on two occasions 50 c.c. of water given subcutaneously produced a distinct increase in the output of urine. However, the normal maximum increase after any given amount of water has been given by mouth takes place forty-five to fifty minutes after the ingestion of the fluid, but in these two cases the subcutaneous injection of 50 c.c. produced an increase which did not reach its maximum until ninety-five and one hundred and five minutes respectively after the injections. Moreover, in both of these instances the animals had been given 100 c.c. of water by mouth five hours previously, all of which was not immediately excreted, so it is reasonable to suppose that in these two instances the tissues were fully charged with fluid, and that the absorption of an extra 50 c.c. from the subcutaneous tissues was sufficient to provoke an increase in the secretion of urine. In no other case did the subcutaneous or intravenous injection of water produce any distinct increase in the amount of urine excreted within three hours from the time of the injection.

I am satisfied as a result of these experiments that the amount of urine excreted depends not only on the amount of fluid ingested but also on the fluid content of the tissues at the time; and even on a regular diet of 500 grm. of moist tripe this fluid tissue content varies somewhat from time to time. Thus on one occasion 50 c.c. of water by mouth was followed by an excretion of 45.52 c.c. of urine in ninety minutes, whereas at another time the same quantity of water produced 29.27 c.c. of urine in the same time, though, as far as one could see, the conditions corresponded in all respects.

Thus it was necessary to determine what was the smallest quantity of water which, when given by mouth, could be relied on to give a

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definite and appreciable increase in diuresis on any and every occasion. After repeated trials I came to the conclusion that 50 c.c. was the optimum quantity to use, working with dogs of 7.5 to 8 kilos, so that the series of experiments constituting this part were all made with that quantity of fluid.

Meyer [3] considers that the cause of the increased diuresis which follows the exhibition of calomel is that fluid is poured out from the tissues into the intestine, part of which fluid is again absorbed from the intestine into the tissues, and that it is this reabsorbed fluid which provokes the increase in diuresis.

In these experiments two dogs were used. Each was provided with a permanent bladder cannula with stop-cock attached, and the technique was exactly as described in the previous paper. It was found that if 50 c.c. of water are given by mouth, there results a marked increase in the amount of urine excreted, having its maximum about fifty minutes after the fluid is given. Similar quantities of water injected subcutaneously or intravenously, with the two exceptions mentioned above, produced no appreciable increase in the amount of urine excreted. A dog was then killed, and its stomach and duodenum immediately excised and thoroughly washed out. This was then cut up into small pieces, which were ground in a mortar with fine washed sand in 200 c.c. of water slightly acidulated with dilute HCl. The extract thus obtained was strained through several folds of muslin and afterwards filtered repeatedly through fine filter-paper. For use this extract was neutralized with  $\text{NaHCO}_3$ , and diluted with an equal quantity of water. The stock of extract was kept in an ice-chamber.

It was found that whereas 50 c.c. of water by mouth produced an increase in the ten-minute excretion of urine from 1.4 to 9.5 c.c. in sixty minutes, 50 c.c. of water injected subcutaneously produced no such effect, the flow of urine never exceeding 2.4 c.c. in ten minutes, and that not until ninety minutes after the injection. When 50 c.c. of the diluted extract of stomach and duodenum were injected subcutaneously the ten-minute excretion of urine rose from 2.3 c.c. to 10.2 c.c., reaching its maximum seventy minutes after the injection. Curves illustrating these experiments are shown in Chart I. Next, a portion of this extract was boiled and again filtered, and 50 c.c. of this boiled extract were injected subcutaneously. There followed no increase in diuresis. In other experiments a portion of the extract was heated on a water-bath at  $59^\circ$  to  $60^\circ$  C. for half an hour, and 50 c.c. of this were injected subcutaneously. Again there was no increase in the amount voided.

These experiments were then repeated on another dog, the extract being prepared in the same way from the stomach and duodenum of yet another dog. The results corresponded in all respects with those just quoted. Chart II shows the combined results of this series of experiments, each curve being plotted out accurately to scale from the figures given by actual experiments.

In order to eliminate the possibility of these results being due to different saline content of the water and the extract, a measured

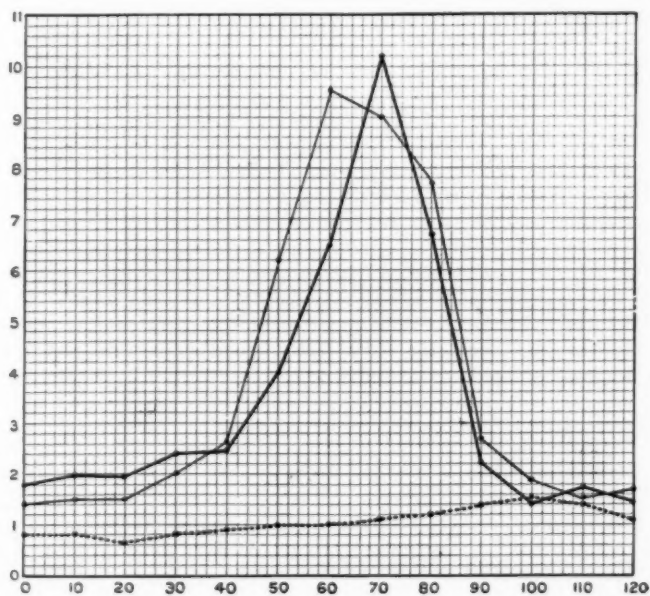


CHART I.

— = 50 c.c. water, *per os*.  
 - - - = 50 c.c. water, subcutaneous.  
 . . . = 50 c.c. extract, subcutaneous.

Ordinate = Urine in cubic centimetres. Abscissa = Time in minutes.

quantity of the extract was evaporated to dryness, and the residue incinerated — so also with equal quantities of the water used and of normal saline solution. It was found that: 100 c.c. of extract contained 0.14 gm. of ash; 100 c.c. of water contained 0.00 gm. of ash; 100 c.c. of normal saline contained 0.76 gm. of ash. Next,

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50 c.c. of normal saline solution were given by mouth, and again 50 c.c. subcutaneously—the results corresponded exactly with those obtained by giving water in the same ways—viz., the saline solution given by mouth produced an increase in diuresis exactly comparable to that produced by the same amount of water, whilst the subcutaneous injections produced no increase.

Barcroft and Straub [1] find that the intravenous injection of Ringer's solution produces marked increase in diuresis in cats and rabbits. Their animals were, however, eviscerated, were under the influence of urethane, and the amount of saline injected, though not definitely stated, was probably very large—"less than the body-weight"!

It seems evident, then, that water given by mouth becomes active in producing diuresis, whilst the same amount given subcutaneously is not diuretic (or, at any rate, only to an inconsiderable extent). Moreover, that some substance, which is inactivated by boiling and by heating at 60° C. for thirty minutes, contained in the gastro-intestinal tract, when added to water, will produce this diuretic effect when injected subcutaneously; moreover, it is not saline content of this which produces the diuretic effect.

Staehelin [5], working on the diuretic effects of various diets both clinically and experimentally on himself, found that meat, fish and eggs produce an increase in diuresis, also that extracts of meat and of fish have the same result. He points out, however, that in the case of these extracts the resultant diuresis is delayed considerably. He shows, too, and Ginsberg also demonstrates the same, that the height of the diuresis produced by taking meat takes place not less than four to five hours after the ingestion of the food, so that if the diuresis produced by extracts of meat is still further delayed, it cannot be the same as the effects which I have obtained, which occur so much earlier. We have, then, circumstantial evidence that the diuretic effect produced by an extract of stomach and duodenum is not caused by extractives of muscular tissue which may be contained therein.

Ott and Scott [4], investigating the diuretic actions of various glandular extracts, found that parathyroid extract gave the greatest diuretic action, and that extracts of other glands, of which the pancreas is one, gave a marked increase in the amount of urine excreted. It is, of course, possible that this substance, be it ferment or not, which is taken up by water during the process of absorption from the alimentary tract, does not produce increased diuresis *per se*,

but that its presence in the tissues after absorption excites the secretion of some gland, possibly of one of those found by Ott and Scott to be diuretic in action. Indeed, the whole matter requires further careful consideration and research; at all events, these results afford strong support to the theory propounded by Meyer (*vide supra*) of the diuretic action of calomel and of other purgatives.

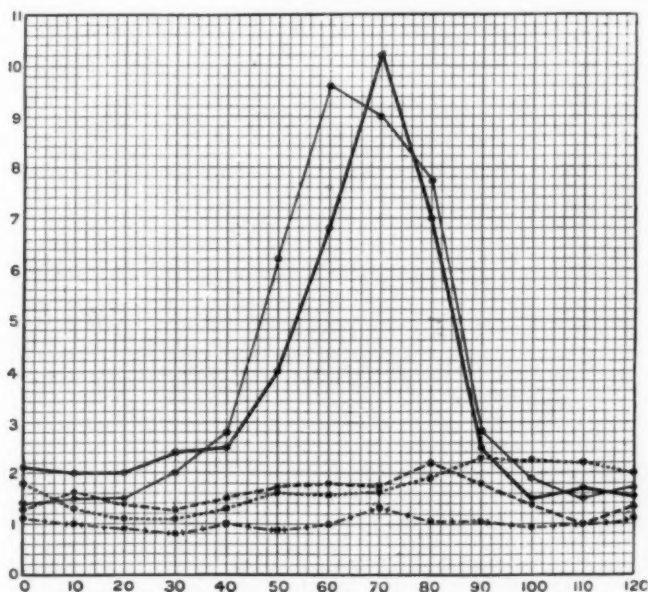


CHART II.

————— 50 c.c. water, *per os*.  
 ..... 50 c.c. water, subcutaneous.  
 —•— 50 c.c. extract, subcutaneous.  
 +—+—+ 50 c.c. extract (boiled), subcutaneous.  
 - - - 50 c.c. extract (heated to 60° C.), subcutaneous.

Ordinate = Urine in cubic centimetres. Abscissa = Time in minutes.

#### CONCLUSIONS.

(1) That the amount of urine excreted after the ingestion of a given quantity of water depends (within limits) not only on the amount of water ingested but also on the fluid content of the tissues at the time.

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(2) That water given by mouth and absorbed from the gastrointestinal tract is incomparably more active as a diuretic than the same quantity of water injected subcutaneously or intravenously.

(3) That there is some substance, possibly of the nature of a ferment, which is taken up by water during the process of absorption from the alimentary tract; and that this substance, either directly or indirectly, has a marked diuretic action.

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## Therapeutical and Pharmacological Section.

January 21, 1913.

Professor W. E. DIXON, F.R.S., President of the Section, in  
the Chair.

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### Discussion on the Non-operative Treatment of Malignant Disease.

Opened by T. J. HORDER, M.D.

THE very fact that we are met here this evening to discuss the treatment of inoperable cancer makes it clear that we lack the essential thing—the knowledge how to cure. If we had this we should have no time to spend on discussions. Yet it should not be thought, on the other hand, that, not possessing this knowledge, our talk must necessarily be futile. One insistent fact alone makes it imperative that we should from time to time consider, and consider even minutely, the means that are at our disposal for the relief of cancer—it is, that the patients are daily clamouring at our door. By free and critical discussion we may hope to arrive at a programme of treatment which shall ensure the best possible relief for the present sufferer, and also yield some hope of cure for the disease in future.

It is to be noted that the title of our discussion concedes the principle that, whatever may be the best method of radical treatment of cancer in time to come, to-day it is by operative removal whenever possible. I doubt if there is anyone here who does not freely subscribe to that principle. To-day is with the surgeon. If this is conceded, it follows that we must not only submit every operable case at the earliest possible moment to the knife, but we must consider, at certain stages in our treatment, whether a case previously non-operable has not now become operable. I take the word "operable" to include any of the means by which total removal of a cancer is undertaken, whether by the knife, by the electric cauter, or by less favoured methods. Thus are



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we hedged about by present necessities; we cannot try any experimental form of cure upon early cases of cancer, because early cases are amenable to surgical interference, and we must not continue a form of inoperable treatment past the point at which operation becomes possible. These limitations are very severe. When we remember how difficult it is to get response to our measures of specific therapy in infective processes that are in an advanced stage, and when we are told that the experimental methods of curing mouse cancer usually fail if the tumour is more than a small percentage of the total bulk of the mouse, we realize the almost insurmountable problem underlying the therapeutics of cancer. But the position must be accepted all the same, and we must make the best of it.

The therapeutics of cancer may be considered to fall under two headings:—

(I) Preventive and curative efforts.

(II) Palliative efforts.

These are, however, not distinct from each other, for some of the efforts at cure relieve the patient's pain and discomfort and prolong his life. On the other hand, curative efforts are sometimes productive of pain and discomfort, and the use of the particular remedies that have this effect should always be considered in terms of the chances of cure *in the particular patient concerned*. A few of the efforts at cure are also used as preventive measures, especially as preventive measures against "recurrence" of removed cancers.

### (I) CURATIVE EFFORTS

may be subdivided according as they are *Rational* or *Empirical*.

(1) Rational efforts may be classified according to the central fact or idea underlying them. Thus we have four of these central ideas, as follows:—

(a) *The Idea that Cancer is due to Errors in Tissue Metabolism capable of Correction by a Diet specially chosen.*—At the Cancer Hospital recently I was associated with Dr. Haig in observing the effect of a purin-free diet upon a selected number of cases of inoperable cancer. The result must be taken as equivocal, because of the great difficulty in persuading patients to give the diet a fair trial. The rationale of such a diet would need to be very convincing to justify its continuance in a wasting and depressing disease, and when faced with further loss of flesh and depression directly attributable to the

diet itself. None of the arguments hitherto advanced has seemed very convincing. Even if it were true that cancer developed more readily in persons who ingested purins, this would surely only be a predisposing cause; we should be still far from a cure by merely cutting out a predisposing factor. And to cut it out with hope of success would seem to require that we start a generation back, if not still further. Almost at the same time that I had arranged to assist Dr. Haig in his experiment I was approached by a physician equally experienced in dietetics, who thought a promising diet for cancer patients was the Salisbury diet, of lean beef and hot water, and wished it made the subject of trial. The very fact that two such extremely opposite forms of diet were advocated as cures for the same disease goes very far to check enthusiasm in regard to either of them. Packard, of Boston, considers cancer to be due to the demineralization of foods, accusing white flour and peeled potatoes as the cause of the disease. Even so, it should be a simple matter to satisfy this observer's desideratum by a full allowance of fresh fruit, by giving wholemeal bread, and by cooking potatoes in their skins. Such considerations leave us still cold. A somewhat more convincing idea, also on the lines of metabolic action, is one that Dr. Monckton Copeman will deal with immediately, and with more authority than I can claim. Dr. Copeman's hypothesis is to the effect that the cancer cell might undergo retrogressive changes if the tissues were denied that principle in food the absence of which leads to scurvy. The diet for a cancerous patient would in this way consist of foods that had been autoclaved, as it is found that such treatment destroys this active principle. I have arranged with Dr. Copeman to give such a diet a trial at the Cancer Hospital.

(b) *That Specific Immunity to Cancer can be established in a manner analogous to Infective Processes.*—It is hoped that either by the use of an anti-serum or of a vaccine the patient may acquire passive or active immunity to the disease. The procedures follow very closely upon those adopted for microbic infections. The excised tumour is macerated, extracted by suitable solvents, and the filtrate is used for hypodermic injection, either into an animal for the production of a serum or into the patient as a vaccine. It is obvious that the living cancer cell cannot itself be injected into the human body, so that it is necessary to use a clear filtrate or the solution of a powdered extract. But that these are capable of inducing cytolytic substances on injection, and that the intact cell is not necessary for the purpose, is rendered possible by analogy with immunization experiments against other cell

structures. The method of active immunization is supported by the experiments on mice, which prove that the animal's resistance to cancer grafts is raised by the injection of embryonic epithelium. Despite a large number of trials, however, little or no success has attended either of these immunity methods in human cancer. This is perhaps the most appropriate place to mention the work of the Grünbaums, who found that the injection of anti-venom (horse) serum effected the regression of inoculated tumours in rats. Their experiments were suggested by the observation that these animals could not retain their susceptibility to cancer grafts, and at the same time be immunized against cobra venom. Professor Grünbaum will be able to tell us of any experimental treatment he has been able to carry out on human cancer, based upon these observations.

(c) *That Radio-activity can lead to Retrogressive Changes in the Cancer Cell.*—Of all the modern methods of dealing with inoperable cancer, the two that have most success to place to their credit are undoubtedly X-rays and radium. They are the most helpful measures in dealing with local recurrences and for application to certain parts that are surgically inaccessible. The choice, as between the two methods, is to be determined largely by the nature and situation of the growth. At the Cancer Hospital we very frequently employ both methods alternately in the same patient, on the principle of combined treatments, to which I shall refer more fully later. Valuable though the application of these rays and emanations are, the limits of their use at present seem all too woefully narrow. A *sine qua non* for radium would seem to be that the growth is on the surface of the body or near to the entrance or exit of the alimentary canal, situations that admit of actual contact by the salt. For Röntgen therapy some greater degree of penetration is possible, and there is hope in the reflection that the experts have not yet exhausted their means of getting still deeper effects by careful choice of tubes and by filtration. Concurrent changes produced in the cancer tissue by some general treatment, as by the use of metals injected intravenously, may quite conceivably supplement the destructive effect of radio-active measures, another effort at combined methods of treatment. But there is one consideration that appeals in disappointing fashion in respect of both these modes of treatment of cancer, and which makes it doubtful if we can expect from them much more than we have already got. This consideration is the great range of their therapeutic use. The very fact that they are of service, and of very great service, in other diseases

seems to impose a limit upon any very selective efficacy in dealing with the cancer cell. That X-ray applications can cause a tuberculous gland to disappear, and a lymphadenomatous one also, and can reduce the size of a leukæmic spleen enormously, seems to argue against that power of specialized effect which we feel essential in a means of cure of so specific a disease as cancer. With radium the comment seems more pertinent still, for it appears day by day more apparent that the action of radium is that of an elaborate caustic upon cancer tissue. But until we know more about the actual way in which these measures produce their effects it behoves us to keep an open mind as to their future possibilities. Neither of them is likely to be *the* cure, be its developments what they may: yet either of them may act as the key that unlocks the door to still more specific treatment. There are reasons for thinking that X-rays produce some at least of their effects by general metabolic changes rather than by local alterations in the cancer cell, that is, they stimulate the general resistance. I think I am correct in saying that marked resorption of recurrent mammary cancer has been observed in patients who have received not local but general irradiation. If the main effect is produced in this way it is easy to understand why the rays should lack specific features for one disease. It has recently been suggested that radium acts by chemical analysis within the cancer tissue, as by liberating choline from lecithin; the choline is then thought to act in a toxic manner upon the cancer cell. The notion has led to the employment of choline directly, by injection, but I have had no personal experience of this method of treatment. I shall leave it to certain of those who follow me to speak of the present, and, as it appears to them, of the future possibilities of these radio-active measures. No doubt by averaging their several opinions we shall get a fair estimate of the position of these valuable remedial agents.

(d) *That the Cancer Cell is more readily destroyed by certain Toxic Agents than are the Cells of the Hosts.*—This is the principle underlying the great majority of the efforts made at curing cancer. We cling to the fact that the cancer cell in its hasty nutrition and its disordered growth is a less stable thing than the cell which it is replacing. It should therefore be more readily destroyed. The natural history of the cancer cell supports this principle, and its inherent tendency to autolysis within the tumour suggests the advisability of trying, by all legitimate means—legitimate, that is, with reference to the tissues of the host—to precipitate this destruction. The various toxic agents that

have been used to compass this desire can be divided into two groups: *microbic toxins*, with which we may conveniently include diastasic ferments; and *drugs*, chiefly preparations of the heavy metals. If we are compelled to regard the chief and ultimate action of radium and of X-ray as of a chemical nature, we must include these measures also under this principle, but it has been more convenient, in the present state of our knowledge, to treat of them separately.

(i) *Microbic Toxins and Ferments*.—Into this class of remedies come Coley's fluid, *Micrococcus neoformans*, and "antimeristem." The observed disappearance of sarcomata during an attack of erysipelas was the pioneer observation which led to treatment along these lines. My own experience of Coley's fluid, using both the market virus and material specially made, has been disappointing at the Cancer Hospital and elsewhere. And considering the fact that this method has been in use now for more than twenty years, and has during this period had very thorough trial, the infrequency with which the treatment is embarked upon to-day is proof of the lack of confidence in it. At the Cancer Hospital, some time ago, I endeavoured to raise the general resistance against streptococcal endotoxin by a preliminary course of vaccine, hoping to prevent some of the severe after-effects of the injections of Coley's fluid. This did actually occur in two cases treated, but only when the doses of the fluid were in the initial small quantities. It would seem that the desirable effects upon the growth are in direct proportion to the degree of general toxicity produced, and that without the general effect the local effect cannot be obtained. The pain and discomfort endured by the patient create, in England at all events, an almost overwhelming objection to the treatment. It is possible that, in conjunction with other methods, such as X-rays and arsenic, doses of lesser size than those producing such acute suffering may be helpful. As I never expected the so-called *Micrococcus neoformans* to do anything which *Staphylococcus epidermidis albus*, of which it is a variant, could not do, I was not disappointed to find, in a series of cases treated at the Cancer Hospital in conjunction with Dr. Paine, that the only good effects were attributable to the operation of a staphylococcal vaccine. I have again and again seen undoubtedly good palliative effects from the use of bacterial vaccines in cancer. The micro-organism most commonly found in, or on the surface of, malignant growths is one or other variety of *Staphylococcus albus*. A course of staphylococcal vaccine will often relieve pain and swelling, assist in cleaning up a discharge, and reduce temperature. But more than this does not seem to occur. I think

there is now fairly universal opinion that the limit of action of *Micrococcus neoformans* inoculation is that of controlling secondary staphylococcal infection of cancer, and that curative effect of the treatment is absent. Of "antimeristem," consisting of a vaccine prepared from a *mucor*, I have had no personal experience, but I cannot find definite evidence that it is of any value. *Diastasic ferments* have been largely used, on the basis of some observations tending to show that the anti-tryptic power of the serum is low in cancer patients. No single method of treatment for inoperable cancer has received a more thorough trial, possibly excepting Coley's fluid, than has the trypsin treatment. Though introduced with much blare of trumpets, and boomed with abundant assurance, it has now sunk almost into the limbo of those many forgotten efforts which lie strewn along the path of cancer therapy. It sought to do too much, and thereby failed at first to evoke even a proper measure of trial; we were warned against a cure being too rapid, and were taught how to salvage the products of cancer destruction by the additional use of amylopsin. Alas! would we could believe that a patient might be killed by excessive zeal in hastening the necrosis of the hostile tissue! Imagine such a thing for one instant; that the only problem left was that of adjusting our remedy so that the cure should be safely slow instead of fatally rapid! Allied to the ferments, perhaps, are certain substances formed in exudates or transudates occurring intercurrently in cancer patients. It has been noted that cancer, on rare occasions, resorbs coincidently with the resorption of such exudates. This observation led to the treatment of cancer cases by injection of the exudate in increasing quantities. One or two partially successful cases have been reported, the most convincing being one in which the patient was so treated with her own exudate. Two years ago, with the help of Dr. Sheffield Neave, I treated six patients in this way with ascitic fluid removed from a woman with metastatic peritoneal deposits secondary to uterine cancer; but we failed to demonstrate any value in the method.

(ii) *Drugs Proper*.—The second group of toxic agents used to destroy cancer cells include chiefly the heavy metals and their compounds. The brilliant work of Ehrlich and his colleagues in connexion with the spirochete of syphilis has breathed fresh life into the flagging body of chemical therapeutics, and has given a great stimulus to research in cancer treatment. A large amount of material provided by many thousands of mice successfully grafted with cancer has been available for the purpose of such research. The highly selective action of various



substances upon particular cells had led to the trial of many products specially synthesized by the chemist for the purpose. Wassermann and others have worked specially with the metals of the sulphur group, and have definitely proved that it is possible to cause the complete resorption of mouse cancer of a certain size by repeated intravenous injection of such a compound as selenium-eosin. Eosin was chosen as part of the metal compound on account of its intensely penetrating character. The demonstration that the cancer cell can be picked out for saturation and ultimate destruction, to the exclusion of the cells of its host, by such means as these, constitutes one of the most significant and encouraging discoveries of recent months. Whether such compounds have any similar effect in human cancer remains to be seen. The choice of the actual compound used is, from analogy with the arsenical preparations employed in the treatment of syphilis, of great importance, and the most efficient preparation—one giving highly toxic effects upon the cancer cell, and relatively low toxic action upon the healthy tissues—may require much exhaustive experiment for its elaboration. Other observers have recorded good results in mouse cancer from the use of tellurium, and from selenium given by the mouth. Copper is also on trial, and Dr. Herschell will tell us of his personal experiences of the colloidal form of this metal. The silicates have had very extensive trial, in the form of simple sodium and potassium salts given by the mouth, at the hands of Zeller and others; and even Czerny is undecided as to whether there is not some curative effect observable from long-continued use of these preparations.

(2) Of purely *Empirical* measures I propose to say nothing; their very name is legion. The *Archives* of the Imperial Cancer Research, judging by Dr. Bashford's historical essay, and of the Cancer Hospital, judging by personal knowledge, are bursting with letters from all over the world, telling of countless "cures," secret and public. Sacks of leaves from the Antipodes cumber the shelves of our dispensary at Fulham. Of one such bag of foliage the enthusiastic writer said: "I purpose to continue sending fresh supplies of this herb until you stop me." The violet leaves, whose reputation lately left its birthplace in Devonshire for a wider sphere, appear to have again retired to the far western country. Nearer home, however, we still have *Alnus glutinosa* with us, and Dr. Underwood Gray, vigorous and confident, to defend it from oblivion. In respect of all such remedies it must always be remembered that to disregard the fundamental criterion is but to confuse the issue and delay our progress—I refer, of course, to the



proof of the diagnosis. Absence of histological evidence, however brilliant the result of treatment may appear, should always call for the exercise of forbearance, and a decision to remain silent. That lump at the pylorus in a wasting patient, not all the opinions of the wisest of us are more than speculation; for a chronic ulcer may produce both signs and symptoms that deceive the very elect, and may yet get well. And so for the mediastinal mass, and for the ragged tongue, so long as there are alternative pathological processes which are capable of spontaneous recovery, with or without the assistance of rest and general treatment, the onus (and a very sacred onus) is with the champion of a cancer cure to make the proof of malignancy complete.

#### (II) PALLIATIVE EFFORTS.

I have endeavoured in my remarks to avoid purely theoretical considerations; a few have, however, been unavoidable. The practitioner in charge of a case of inoperable cancer is only helped directly by what is practical. There are really very few cases in which there is nothing to do except negotiate euthanasia, though in the vast majority of patients this stage of the treatment arrives sooner or later. Whether a definite effort should be made in a curative direction depends much upon the nature and position of the growth, and the general state of the patient. As already indicated, it is desirable to choose those means of so-called curative treatment which carry with them relief of distressing symptoms. I am fully convinced that *the most satisfactory line to adopt in most cases is a combination of several different measures.* Not in a state of panic, but with deliberate choice of a programme. Thus, faced with an inoperable sarcoma, it might be good to lead off with an alternation of X-rays and radium, and, as an intercurrent measure, give two or three doses of salvarsan intravenously at weekly intervals. In dealing with one of the most common of all types of case, that of a woman who has had a breast removed and has developed recurrence that is inoperable, X-rays and radium may again be employed; vaccines should be given if there is ulceration and evidence of secondary infection, the diet may well be regulated on the basis already indicated and general tonics employed. The question is sometimes raised, whether any preventive treatment should be employed—as by radio-activity—after the operative removal of a cancer. Some Continental authorities advise that the scar be treated in this way for some weeks following the operation. A few go as far as to

advise keeping the wound open for a time and subjecting it to X-ray applications. This does not appear to have met with much support in England.

Partial removal of fungating or ulcerating growths may be included amongst methods of inoperable treatment, since we have defined "operation," for the purpose of this discussion, as complete removal. Such partial removal is sometimes of very considerable service, and the resultant improvement in the patient's condition may be most marked. It allows of the removal of obstructions—e.g., in the mouth—and of a cleaner and less septic surface. The good effect upon the mental state is also sometimes marked. In this connexion Mr. Harmer will give us his experiences of the use of the diathermy method of treatment in mouth and throat cases.

In the *relief of pain* it must, first of all, be carefully determined what the immediate cause of the pain is—whether gross pressure or infiltration, or secondary inflammation. Aspirin and others of the coal-tar products will often relieve pain without the use of opium. The relief of pain due to infiltration and pressure, by the use of X-rays, is often most marked, and very severe neuralgias may sometimes be assuaged by this means. The customary antiseptic and analgesic lotions must be applied for discharging surfaces, and the use of a penetrating vehicle, such as acetone, is often very useful, especially in vaginal and uterine cases. Sanitas, by virtue of its peroxide, is a most useful wash and deodorant. The field of mental therapy must not be overlooked. But here it is very difficult to offer advice. The personality of the practitioner and the philosophy of the patient are the medicines that are available. Two lessons we all have probably learnt: that not every patient who "wants to know the truth" is prepared to hear it, sometimes he least who asks most boldly; and that self-deception is not seldom a valuable analgesic well worth preserving.

#### CONCLUSION.

I will not stay to labour the obvious fact that in the matter of curing cancer our efforts have scarcely even begun to receive reward. The sun has not yet risen—the proper metaphor is less than this even—there is, as yet, no glimmering of the dawn. An occasional meteor there is, a flash in the darkness, causing the foolish to cry "Lo! here is the day!" But that same instant it is gone and the place thereof knows it no more. In the absence of facts it is always easy and tempting

to be sententious, and no subject so leads to words that are rich in judicious observations, but poor in everything else than words, as does the problem of cancer. All the same, it is imperative that we should keep our attitude right, and the right attitude I take to be divine discontent with the present, patient toil, free exchange of views and results, and an open mind. Such an attitude will assuredly lead us to knowledge at last. Every field of human endeavour must be utilized, for we know not from which quarter help may be forthcoming, whether from the biologist, the chemist, the physicist, the pathologist, or the clinician. The proper equipment of a cancer institute includes all these, and with such organization as will get the maximum efficiency for each. I should like to give one word of advice and encouragement to the clinician. Yours is the brunt of the dreary day-by-day conflict with the disease. Do not merely watch eagerly for those isolated pieces that emerge periodically from the research laboratory, endeavouring to fit them into the therapeutic puzzle. And still less do not wait for a full revelation of the complete picture. It may be with you, after all, with your bedside observations, and with your efforts at treatment according to present knowledge, that the key of the problem of human cancer rests. Out of such observations and out of the results of such treatment may arise, not only treatment more perfected but actual elucidation of the cause of the disease.

Dr. S. MONCKTON COPEMAN, F.R.S., expressed his indebtedness to the officials of the Section for affording him the opportunity of placing before it a brief résumé of the results of research work on various lines in which he had been engaged during the small amount of spare time which his official duties had allowed, in the course of the last nine or ten years. Like everybody else, he was much interested in the possibilities of the cure of cancer; indeed, who could fail to be so when they reflected on the sacrifice of life from cancer at the present day, as shown by the Registrar-General's returns. The disease was one more particularly of middle life and the years following, and it was a depressing fact that of individuals reaching the age of 35, one in seven women and one in eleven men would, under existing conditions, presently die of the disease. Therefore, looking at the fact that, notwithstanding the magnificent work being done at the numerous well-equipped institutions for cancer research, practically no indications as to a specific method of treatment had as yet been obtained, he had thought, for many years past, that it was desirable, and even advisable, to endeavour to

carry out any line of work, having possible bearing on the treatment of the disease, for which there seemed any reasonable basis in theory. He had, therefore, from time to time, investigated a considerable number of different methods, in addition to that to which Dr. Horder had just referred. It was only fair to say that accomplishment of the work would have been quite impossible but for the great help which he had received from numbers of people, among whom he would specially mention his old friend and former pupil, the President of the Section, who had most kindly afforded him the hospitality of his laboratory at Cambridge for the carrying out of any work involving controls with mice, &c. He also wished to say that he was indebted to several of the great manufacturing firms<sup>1</sup> for providing him with material, often specially prepared, for use in research work or treatment, without cost of any sort. Dr. Thackray and other of the Superintendents of the Metropolitan infirmaries, institutions in which there existed wonderful mines of clinical material which were practically never worked at all, had also afforded him special facilities; and to anticipate criticism in this connexion he wished it to be clearly understood that where the work had involved treatment of the human being, that had only been carried out with the full co-operation of the patient and his or her medical adviser.

Dr. Horder very properly referred to the difficulties one met with in carrying out any work of this kind. First, it was essential that one should have a definite diagnosis. This he had always borne in mind, and, as a preliminary to any experimental work on the human subject, he had always endeavoured to establish it, so far as possible, both clinically and microscopically. Again, only patients in whom the growth was more or less external and visible, including growths about the mouth or other orifices, were dealt with, so that one might be able to judge accurately of the results obtained. Records, measurements and photographs had been kept, and tracings on tracing cloth were found very useful, as this material could be disinfected, and by superimposing the tracings of one date over those of another date a very accurate estimate of variations in one or another direction could be gained. Furthermore, it must be borne in mind that a certain number of tumours, even including those which were undoubtedly malignant, tended to retrogress spontaneously. That point was not, he thought, sufficiently recognized; and of course it constituted an obvious trap for the unwary, because if one happened to be using any

<sup>1</sup> More especially Messrs. Parke, Davis and Co., Messrs. Burroughs Wellcome and Co., Messrs. Martindale, and Messrs. Squire and Sons.

particular method of treatment during the course of which this change came about, obviously the treatment being pursued at the time would tend to get the credit. On the other hand, the fact that these growths sometimes not only retrogressed but even disappeared, was one of considerable encouragement. Because, although he knew that Dr. Williams and others were of opinion that there was nothing specific about this retrogression when it occurred, he (Dr. Copeman) could not help thinking that there probably was, and consequently, if they were able, in due course, to determine the methods and conditions under which Nature was capable of dealing in this way with what was obviously a malignant growth, then by following similar methods equally good results might eventually be procurable. He was sorry to say that, up to the present, none of the work which he had carried out could be said to have had any permanently good result in the cure of patients, but in that respect he supposed his case was not peculiar. Nevertheless, he thought it might be well to give a brief account of some of the work which had been carried out, mainly with the object of preventing other investigators wasting a great deal of time and trouble over work which had already been tested, because he believed he had been an honest critic of his own work, and that what had been done was carried out very thoroughly.

Some of the work had been purely empirical, and of that he would not speak on the present occasion. And he would also pass over much of the work that he had carried out, including the use of various thymus extracts, concerning which, it was interesting to note, that when more than a year's fruitless work had been accomplished there appeared in the papers a notice stating, on the authority of Sir Frederick Treves, that the successful treatment of cancer would probably be found to lie in the use of preparations of the thymus gland. He now gathered from Dr. Horder's remark that the use of salvarsan had been favourably regarded. In this connexion he might mention that, shortly after the work of Ehrlich involving the treatment of syphilis with salvarsan had become known in this country, he (the speaker) was discussing the question of cancer with Mr. Plimmer, so well known for his researches in connexion with the histology of cancer, whom he found still of the opinion that a parasite was probably concerned in the production of malignant disease, not necessarily bacterial, but possibly rather protozoal in nature. Consequently, as it had already become known that salvarsan had afforded definitely useful results in several protozoal diseases, other than syphilis, Dr. Bernstein and he (Dr. Copeman) took

the opportunity of inoculating a number of cancer patients with this substance, but he regretted to say that, so far as they were able to judge, no improvement resulted in the condition of any of the patients.

On the suggestion of Professor Dixon, in the course of some experiments which he (the speaker) was carrying out in the pharmacological laboratory at Cambridge, and in view of the marked influence of calcium salts on young tissue, they inoculated a number of "cancer" mice with calcium lactate, treating at the same time a second set of mice of equal age by means of inoculations with sodium citrate, keeping as controls a third set to which nothing was done. He confessed that they were somewhat astonished to find that, at the end of a considerable period, there was no appreciable difference between any of these three sets of mice. Calcium chloride and the hypochlorites, for various reasons which he would not now go into, were also employed.

Wherever it had been possible, work on the human had been controlled by work on mice, although, partly as the result of a lengthy research on hydrochloric acid in the stomach in cancer, carried out by himself and Dr. Hake, the details of which had been fully reported in the *Proceedings of the Royal Society*<sup>1</sup> and in the Third Scientific Report on the Investigations of the Imperial Cancer Research Fund (1908), he did not think there existed so complete a parallelism between the so-called experimental cancer in the mouse and that of the human being as had been very generally assumed. It might not be generally known that, as long ago as 1842, the late Mr. Golding-Bird, of Guy's Hospital, pointed out that practically no free hydrochloric acid could be demonstrated in the stomach contents of patients suffering from cancer of that viscus. A number of observers since that date had confirmed this observation, but it was only within the last few years that Benjamin Moore, Walker, and others showed that it apparently held true also when cancer affected any other part of the body. After discussing the matter with Dr. Bashford, he determined, with the help of Dr. Hake, to see to what extent that diminution or disappearance of hydrochloric acid in the stomach in cancer occurred in the case of the experimentally inoculated disease in the mouse. It was a rather difficult matter to compare their observations directly with those of previous investigators, because, as being of much more importance than the estimation of the so-called free HCl, they determined the amount of physiologically active acid. At first estimations were carried out on batches of mice, but later they found methods of testing

<sup>1</sup> *Proc. Roy. Soc. Lond.*, ser. B, 1908, lxxx, pp. 444-62.



the amount of physiologically active HCl in the stomach of a single mouse. It was found that, instead of there being, as in the human subject, a diminution of hydrochloric acid, there was an increase. In the Guthrie Lecture<sup>1</sup> at Westminster Hospital in 1907, Dr. Copeman referred to a suggestion by Dr. Bashford that this increase in HCl in the stomach of the "cancer" mouse was an attempt on the part of the organism of the mouse to deal with more proteid, which was wanted for the nutrition of the mouse *plus* its tumour, and stated that it would be desirable to see if the same conditions obtained in spontaneous cancer in the mouse. He was enabled to investigate this point eventually, through Dr. Bashford kindly supplying stomachs of mice which had suffered from spontaneous cancer; and in them also there was found a definite increase of physiologically active hydrochloric acid. In the case of the human subject, however, as the result of very many experiments, it was determined that the amount was almost invariably deficient. He thought that possibly, if the trypsin treatment of cancer was at all serviceable, one might get at any good which was thereby likely to be obtained, in a more reasonable way, by supplying the hydrochloric acid which was lacking in most cases of human cancer; because one knew, from the work of Starling and Bayliss and others, that if there was a deficiency of hydrochloric acid in the stomach, it was likely to be the beginning of a vicious circle of digestive metabolism in which the pancreas was involved. It was the exit of acid chyme from the stomach which started the flow of the succus entericus, and also the pancreatic juice by causing the formation of secretin. Therefore, if, in any particular instance, increase of trypsin was likely to be serviceable in the treatment of the disease, it seemed feasible that by giving hydrochloric acid by the mouth one might, to some extent at any rate, supply that need. Consequently, whenever examination of a test meal indicated definite diminution of physiologically active HCl, it would surely be reasonable, in connexion with any other treatment which might be employed, to endeavour to bring up the amount of hydrochloric acid in the stomach during the process of digestion as nearly as possible to the normal. Professor Dixon had told him that in all probability no harm would result from the continuous administration of at any rate 15 minims of dilute hydrochloric acid, prior to every meal in the day, in such cases.

Another method of which he wished to speak consisted in the removal of a certain amount of blood by venesection, followed at intervals by re-inoculation into the body of serum from the blood thus obtained.

<sup>1</sup> *Practitioner*, 1907, lxxix, pp. 185-202.



Working in conjunction with the late Mr. Leaf, and with Dr. Paine, at the Cancer Hospital, several patients were treated by this method two or three years ago, and the results were brought forward at a discussion in the Section of Pathology of this Society. There were described the preliminary results of several cases, particularly some in which there had existed considerable œdema of the arm in connexion with breast cancer. In these the favourable results following on venesection were astonishing. The withdrawal of 10 to 13 oz. of blood from the opposite arm to that affected was followed in the course of a few days by an enormous diminution of the œdema, so that, in one instance, a woman who said she had not seen her knuckles for six months was, four days afterwards, at the Cancer Hospital, helping to take her food with the hand which had been previously useless. The blood was, in each instance, taken aseptically from a vein, and some of it was kept in flasks in an ice-chest for a long period, during which it still remained absolutely sterile. On testing the reaction of the serum this was found to be so markedly alkaline in these cases as to give a definitely blue coloration to ordinary litmus paper. This high ratio of alkalinity seemed not improbably to have some relationship to the diminution of hydrochloric acid observable in the stomach in cancer, and it might also be thought of as being connected with the well-known results of Loeb, who had shown that an increase of alkalinity, within certain limits, is capable of exerting a great effect in accelerating the growth of undifferentiated cells. A number of inoculations of the serum of the blood were subsequently carried out both on patients from whom the blood was obtained and on other patients, but, so far as he could see, not with any eventually beneficial result, although, for a period of several months, all these patients who had been bled on one or more occasions were positive in their statements that they had derived great good from the procedure, quite apart from the question of lessening œdema. But, unfortunately, they all died eventually, one from sudden hæmorrhage. In some instances, however, the area of growth was, for a time, considerably diminished.

The remaining work which he had done dealt with the use of various substances derived from the reproductive glands; and the employment of various "deficiency" diets to which Dr. Horder had referred. The work with the products of the reproductive glands was based on various observed facts which could be gleaned from the Registrar-General's returns, and on other experimental work by numerous observers, which tended to show that apparently there was some relationship between the age at which cancer ordinarily appeared and senescence of certain of the

tissues. It was curious that cancer was a disease more particularly of certain ages, those ages when, in all probability, the reproductive functions were tending to wane, but it was not a disease necessarily of old age. He did not suggest that the sexual organs, as such, had anything to do with the prevalence of cancer, but he thought it possible that certain metabolic changes in the body, which might be connected with the absence, or an abnormal condition of, say, an internal secretion of the reproductive organs, might play a great part in the appearance and control of cancer.

Various other points occurred to one as seeming to throw light on this fact. It would be remembered that when work on experimental cancer in mice was first introduced it was found exceptionally difficult to carry on the strain in many instances, and Dr. Bashford had told him this was probably for the reason that, as cancer was a disease of advanced life in the human, mice as old as possible were used, at first, with the result that success was obtained in only a few instances; while, on the contrary, when animals of not more than 6 or 7 weeks old were used, the percentage went up at once, and now it was not infrequently possible to get, with certain tumours, 100 per cent. of successful inoculations. In this connexion it was worthy of note that the mouse did not become sexually mature until it reached the age of about 6 months. Every possible derivative of the sexual organs had been used, including spermine, which was believed by Pöhl and others to constitute the essential factor; and also nuclein and allantoin. But no encouraging results were obtained, and allantoin was found to produce a definite increase in the growths. Thinking that in all probability the factor must be a chemical one, and due to some perverted metabolism of the body, when Holst and Frölich, and others, first directed attention to the "deficiency diseases," he came to the conclusion that one might obtain some useful result by utilizing the outcome of that work. Dr. Hopkins, of Cambridge, with whom he had had numerous conversations on the matter, had found that by removing some definite nutritive factor from food, something which was almost inappreciable in amount (as in the case of the substance present in an extract of rice polishings, the absence of which gave rise to the disease known as beriberi), it was possible to produce an enormous difference in the nutrition of the body, especially in young animals. What, therefore, he (Dr. Copeman) desired to see carried out on a more extensive scale was the trial of a diet from which those bodies termed *vitamines* by Funk, but for which the term "*trephones*"

would, perhaps, be more appropriate, had been excluded, because it was found that whereas their presence had a great effect on the growth of young and embryonic tissues, they had but little effect upon those of older animals. In cancer as met with in the human subject those two conditions were combined; there were the adult tissues of the body of the host which were not increasing to any extent now, whereas there were also the young and rapidly growing cells of the cancer. Therefore there was some *prima facie* suggestion that one might be able to obtain a differential action on the cancer cells as opposed to that on those of the body generally. And evidence was now available that that was, to some extent, the case, for already they had had certain cases under treatment at St. Pancras Infirmary where, however, at one stage of the work they unfortunately included in the dietary certain substances (not then understanding the details of the problem entirely) which subsequently proved to contain these "trephones" in considerable amount. Previous to this the Medical Superintendent was definitely of the opinion that a certain amount of improvement was obtained; but whether and to what extent that would be found to be so when a large number of patients came under treatment remained to be seen. But there was obviously reasonable ground for attempting the method on a larger scale than, up to the present, had been practicable; and he was much indebted to Dr. Horder for his promise of facilities at the Cancer Hospital to enable it to be put to an exhaustive test in practice.

Professor A. S. F. GRÜNBAUM: The remarks which I wish to offer concern the treatment of new growth by means of serum and of vaccine. Some nine years ago I tried the serum from a mare affected with epithelioma of the vulva on a human case of uterine cancer. There was a very marked reaction and each injection was followed by a rigor. The uterus became much more movable and could have been operated on if the patient had consented. When she first came into the Poor Law Infirmary it was absolutely fixed. I have also tried the effect of the serum of cows inoculated with human mammary cancer on human cases of cancer of the breast, but without effect. More recently, Dr. Helen Grünbaum and I have tried certain other sera, with which we were led to experiment from the following considerations.

We found that rats affected with inoculated rat sarcoma, were abnormally sensitive to cobra venom and that it was not possible to immunize that against this venom. We deduced from this that

some substance which would usually protect them to some extent against cobra venom was absent, and that this absence had something to do with their susceptibility to rat sarcoma. Since experiment had shown that it was very difficult actively to immunize such tumour-bearing rats against cobra venom and immunity to cobra venom appeared to be correlated to refractoriness to inoculation with sarcoma, we tried passive immunization with anti-venom serum and found in a considerable percentage of cases that the tumour regressed. A later series, in which we added adrenalin to the anti-venom serum produced even more successful results, and we were able to cure about 70 per cent. of rats in which the tumour exceeded 1 c.c. in size at the commencement of treatment, and, as the control series showed, most of them would almost certainly have continued to grow. This marked result led us to try the treatment on human cases. The first, a case of recurrent sarcoma of the cheek, diminished remarkably in size during the three weeks that we gave the serum, and the patient altogether improved greatly in condition. We then attempted to continue the treatment by active immunization, but this was a failure, and on resumption of the serum treatment some months later, under difficulties on account of anaphylaxis, it had no further good effect. In another case in which the leg was amputated for periosteal sarcoma at the lower end of the femur, we treated the patient for a few weeks with serum, and since then, for over a year, we have given small doses of cobra venom to keep up the immunizing condition. It is now sixteen months since the operation and so far there is no evidence of recurrence. It should perhaps be mentioned that the condition of immunization against cobra venom can be tested without much difficulty, by the anti-hæmolytic power of the serum to cobra hæmolysis. The details of this test have been published elsewhere and would take too long now to describe. Suitable cases of sarcoma, which the surgeons feel justified in relinquishing, are not very common, so that we have not yet many instances. We expect that it is especially in the cases of spindle-cell sarcomata that the treatment will be of use, because it is a spindle-cell sarcoma in the rat which seems specially amenable to the anti-venom serum.

The origin of this serum treatment then rested on an experimental basis. Its further extension depended partly upon hypothetical and partly upon experimental data. On the hypothesis that any form of irritation may lead to new growth, provided the tissue were in a susceptible condition, we thought that certain tissues being often

affected, or liable to be affected, with certain bacteria, the anti-serum to such bacteria, or a vaccine made from the bacteria, might be efficacious. For instance, in the case of tissues liable to the presence of diphtheria bacilli, the employment of anti-diphtheritic serum might be of use. This assumption was corroborated when we found that the process of suppuration would lead to susceptibility towards inoculation with sarcoma in some rats which had previously been refractory. Consequently, we tried the use of anti-diphtheria serum in a case of carcinoma of the larynx in man, with very striking results. The patient put on nearly a stone in weight during the time that we were able to administer the serum and his subjective condition greatly improved. He had, however, a bad anaphylactic attack after six weeks' administration and we were then obliged to discontinue its subcutaneous use. From that date he regressed, in spite of the employment of diphtheria vaccine and, later, serum by the mouth. We were not able to test his immunity towards diphtheria, so it may be that the vaccine even did him harm.

Another case of cancer of the breast, which gave no marked hæmolytic reaction with cobra venom, we treated first with cobra anti-venom serum and then with viper venom vaccine (because the blood gave a hæmolytic reaction with viper venom) and X-rays. This case, which was regarded as inoperable by the surgeon, had a tumour surrounded by a circle of small nodules, which have all disappeared, and the main tumour is much more movable than it was. The patient has been under treatment for some nine months and has not lost weight, in fact, has gained a pound or so during that time. Of course, we do not ignore or depreciate the effect of the X-rays. Two cases of gastric carcinoma have been treated for five months with viper venom and their condition has much improved.

This form of treatment is quite in its infancy, but from the results so far obtained it seems to be worth while trying it in more cases. There is an important point about it, upon which I think its success or failure will largely depend. If the size of the tumour is so great that a very large number of cells have to be destroyed by the serum or the reaction to the vaccine, I think it likely that the surviving new growth cells may become immune to the treatment. Consequently, for its success it would seem that so much of the growth as can be surgically removed should be taken away, and then the therapeutic treatment taken in hand and maintained. Further, it may be desirable to persist with prophylactic inoculations of the vaccine for some time after the tumour has apparently disappeared.

One other experimental fact is perhaps worth noting in this connexion. We have found that the administration of virol, which we gave with the idea that it might possibly lead to a diminution of the growth, appears, at least in rats, rather to accelerate it. We should very much like to know whether any clinical results of this kind have been observed.

MR. DOUGLAS HARMER: Mr. President, I must thank you for the invitation to join in this discussion. I propose to speak on the treatment of malignant disease of the mouth and pharynx by diathermy. The apparatus which is seen here produces a high frequency current of great power. It has two electrodes, a large one which is wrapped in wet towels and laid on the patient's chest or abdomen; the smaller one, which has a metal end, is plunged into the growth. The passage of such a current through the small electrode produces intense heat which rapidly destroys the tissues. On the other hand, very little heat is produced in the region of the larger electrode, because of its greater size, and because it is kept cool with wet cloths. The details of treatment are as follows: A general anæsthetic is required. The growth must be sponged so that it is quite dry. The electrode or needle is plunged into the growth, and the current is turned on for three to five seconds, by which time the neighbouring tissues are dead. A series of punctures is made so that every part of the growth is attacked. This can be done in about five minutes. There should be no bleeding even with vascular tumours.

During the last eighteen months I have treated eight cases of inoperable carcinoma in this way. The growths have involved the palate, tonsil, base of tongue, and pharynx. They were considered too advanced for operations with the knife. There has been very little pain even after extensive destruction of tissue, and the patients could swallow reasonably in twenty-four to forty-eight hours. It is remarkable that the surrounding tissues do not become much inflamed; there appears to be no tendency to an œdema such as occurs with milder forms of burning. The sloughs have separated in five to ten days, leaving a healthy wound without discharge. The wounds have been covered with soft mucous membranes, and there has been no tendency to scar formation when the whole of the growth has been destroyed. There has been no shock, and the patients have not been confined to bed for more than twenty-four hours. There has been nothing suggestive of secondary hæmorrhage, and no other complication, such as burning in the region of the



larger electrode. In most cases more than one operation was found to be necessary.

All the patients were definitely improved by the treatment. The best result was obtained in an old man with a growth on the front of his tonsil and adherent to the upper and lower jaws. Three applications were made, and he now appears to be well, fourteen months after the first. The second case was reported well seven months after treatment. Two were only improved temporarily. The fifth case had a rapid recurrence. The sixth is still under treatment. The seventh case, with carcinoma of the cheek afterwards, had the growth excised, and the last, with carcinoma of larynx and pharynx, died about three weeks later. After the burning the patient appeared to be doing well, and about half his growth seemed to have been destroyed. He left the hospital after a week. When written for later he was reported to have died of septic pneumonia, but it was uncertain whether this had any connexion with his treatment. In two of the above cases in which the primary ulcer was destroyed by burning I removed the cervical glands by a second operation. In the second case radium treatment was given by Dr. Finzi, and the patient was so improved after five months that he was able to go to India without any obvious growth.

My impression is that diathermy is suitable for the destruction of massive ulcers in mouth or pharynx associated with urgent dysphagia, blood-spitting, or constant expectoration. There appears to be no difficulty in destroying the superficial parts of such a disease, and the throat is more comfortable afterwards. There is no evidence which leads me to think that the cancer cells are more easy to kill than normal tissues. It is possible that there is less tendency to recurrence than after a cutting operation. I have noticed that in some of the cases where growth remained it became atrophic in character. It is yet too early to say whether the method will be valuable for treatment of earlier growths, or whether it will be as good as the knife in this or other parts of the body. The obvious advantages are the rapidity of the operation, the possibility of removing a dangerous growth without loss of a single drop of blood, and the fact that the vessels and lymphatics are sealed by the burning. In any case, we have in diathermy a method of dealing with malignant growths in the pharynx which is worth consideration.

Dr. GEORGE HERSCHELL: During the last year a considerable amount of work has been done in the treatment of cancer by colloid copper, and I do not think that it should be passed over in this



discussion without careful consideration. I am able to find histories of fifty-three cases reported in the French medical press in which a cure was claimed in fourteen cases (26·7 per cent.) and improvement in thirty-six cases (57·9 per cent.). In three cases no good appears to have resulted. Making every reservation for unreported cases in which success was not obtained, I think that we must admit that some good results have followed the use of colloid copper in cancer unless we are prepared to assert that all the medical men who have reported these cases are engaged in a gigantic conspiracy for their own ends to delude the medical public of all nations. In some of the reported cases the diagnosis is, I admit, open to question. For instance, one case, in which a cure followed the treatment, was obviously one of duodenal ulcer and not cancer of the stomach. But in others, in which equally good results have been reported, the diagnosis was confirmed by men of the very highest standing.

There are two kinds of colloid copper. The electrically prepared colloid which is manufactured by passing an electric arc through copper plates immersed in water, and the chemical colloid which results from the slow reduction of copper in the presence of albumosic acid. Theoretically the electric colloid should prove most efficacious, as the particles of copper are reduced to the finest state of subdivision. Clinically, however, the chemical colloid appears to give the best results. In the following cases, chemically prepared colloid was used. Experimentally it has been proved :—

- (1) That particles of colloid copper can be demonstrated in the granulations of cancerous growths after two or three injections of the colloid; and clinically
- (2) There is invariably great relief from pain.
- (3) Appetite and strength return, and the patient puts on flesh.
- (4) There is in many cases a diminution in the size of the tumour.
- (5) The injections are absolutely non-toxic, although in many cases an inflammatory reaction is manifested in the cancerous growths.

As regards my own personal experience in the use of this method of treatment in addition to my own cases, I have had an opportunity of observing the effects in the practice of some of my medical friends, and in nearly all cases the progress of the disease appeared to be arrested.

The cases which have been under my own care are few, and from the special nature of my practice confined to cancers of the gastrointestinal tract. Such as they are, however, they are of interest. My excuse for publishing them at such an early stage of their treatment is,

first of all, to make this evening's discussion as complete as possible, and, secondly, to encourage medical men to make an early trial in similar cases of a method which is quite harmless, and possibly of extreme value, and which will not interfere in any way with any surgical measures which may be adopted.

Mr. P., aged 40, came under observation in August, 1912, and is still under treatment. When he was first seen he had just had a serious hæmorrhage from the stomach. He was obliged to go to Germany after a week's treatment in bed, where he had a second hæmorrhage, and consulted one of the leading gastrologists in Berlin, who pronounced his affection cancer of the stomach. He consulted me again in December, 1912, when I found that his weight had fallen from his normal (15 st.) to a little over 13 st. He was so weak that he could hardly walk and had constant vomiting (this occurring after nearly every meal). He also complained of a dull, constant pain in the epigastrium. On palpation a distinct tumour could be made out above and to the left of the umbilicus. Treatment was commenced at once with injections of colloid copper every fourth day. From that time, the improvement has been continuous and without any break. His weight has steadily increased up to 14 st. 8 lb. which is probably normal for his height and physique. The appetite has returned, pain and vomiting have ceased, and on examination a few days ago no tumour could be made out in the abdomen. In fact, the improvement has been so very great that the man is making arrangements to resume his occupation of a variety artiste. He says that he feels better than he has done for ten years.

Now, it is difficult to see what affection this could be other than malignant disease. Simple gastric ulcers do not come in men of his age, the time relation to food, characteristic of the pain of duodenal ulcer, was absent, also pain on pressure in the region of the duodenum or appendix. *Per contra*, a progressive anorexia and weakness, with hæmatemesis, progressive loss of flesh, vomiting, and constant pain, with a distinct tumour, should, I think, justify the diagnosis of malignant disease.

As regards the part played by the copper in the cure. Here we have a man steadily going downhill. From the moment that this particular treatment is commenced he began to improve. If this occurred in one case only we might assume a spontaneous retrogression. But when the same result occurs in two or more cases the possibility of such an event is materially reduced, and we are forced to admit that the copper *may* have something to do with the improvement.

J. W., aged 63, came under observation on August 10, 1912. For the last few months he had been losing flesh, appetite, and energy. Latterly he had been vomiting after nearly every meal, and had had more or less continuous pain in the region of the stomach. On examination a tumour can be felt between the umbilicus and the ensiform cartilage about the size of a tangerine orange. There is marked anæmia, the red corpuscles being 3,500,000 per cubic millimetre, and the hæmoglobin 36 per cent. The patient is only just able to walk, and becomes very short of breath on the slightest exertion. Treatment was commenced on December 4 with injections of colloid copper into the deltoid. The patient has steadily improved. On January 14, 1913, when he left the nursing home, there had been a total gain in weight of 18 lb. The appetite is good, the blood corpuscles are 4,300,000 to the cubic millimetre, hæmoglobin 64 per cent. Vomiting is entirely absent, and the tumour has much diminished in size.

Mr. S. aged 59, sent to me by Dr. Pugh, of Bream. For the last two months had had constant pain in the region of the stomach, and vomiting after every meal. Weight had fallen from 13 to 10 st. On palpation a distinct tumour could be made out, corresponding in position to the stomach. The colour of the skin was yellow, and there was marked anæmia, the red corpuscles being 4,360,000 per cubic millimetre, and the hæmoglobin 38 per cent. The patient was taken into a nursing home, and treatment commenced on December 19. Improvement has been continuous, vomiting ceasing on the second day, and on January 13, when he left the home, the weight had risen to 11 st. No pain or vomiting. The tumour was apparently reduced to half the size.

To take the last case which I have had, and which is yet only at the commencement of treatment, the result is undoubtedly good enough to encourage hopes that permanent benefit may ensue.

Mr. J. N., aged 58, scaffolder, whom I first saw on January 1, 1913, has had an aching pain in the epigastrium for six months. For the last six or seven weeks he has vomited nearly every meal. His weight has fallen from 14 st. 2 lb., three months ago, to 10 st. 5 lb. on January 1. The vomiting occurred shortly after taking food, and was evidently not the result of pyloric stenosis. The patient was markedly anæmic, the red corpuscles being 3,400,000 and the whites 6,000, of which lymphocytes accounted for 42 per cent., polymorphonuclears 56 per cent., and eosinophiles 2 per cent.; this

preponderance of lymphocytes being, of course, strongly suggestive of malignant disease. Upon palpation a tumour could be made out above and to the left of the epigastrium measuring roughly 2.1 in. The injections of copper colloid were commenced on January 1, and continued every four days. To-day (January 21) the pain is much better, the vomiting only occasional and after a badly prepared meal, and the weight has risen to 10 st. 1 lb. The patient feels much stronger and better, and has lost his yellow look. The tumour is apparently about half the original size.

In this case, if we admit the diagnosis, which I think that we must do, copper has already certainly had a definite effect.

In conclusion, I am afraid that there will be considerable difficulty in establishing whether or not colloid copper will actually affect a permanent cure in cancer, the reason being that each dose costs 2s. 6d., and must be given at least once a week with, of course, the doctor's additional fee for injecting. This, for instance, will prevent its being placed on the list of methods sanctioned by the Insurance Commissioners. As a matter of fact, even moderately well-to-do people can only with difficulty be induced to continue the treatment after a certain amount of improvement has been obtained. The injection, which measures 2 c.c., should be given into the deltoid or into one of the glutei muscles at first every four days; later on the interval may be increased until the injections are only given once in seven or eight days. If any local reaction is observed the time between the injections should be temporarily increased.

Dr. LEWIS JONES: I approach the discussion of this problem with great hesitation, for it seems to me that in spite of all the work which has been done in the application of X-rays and of radium to cancerous cases, we are still baffled in our efforts to understand exactly what is the mode of action of these agents, or to obtain results which are convincing. I confine my brief remarks to X-ray treatment, because my experience with radium is too slight.

The points on which X-ray treatment in cancer was based are as follows: X-rays can lead to the cicatrization of a chronic ulceration existing in the scar of a cancerous site, and the melon-seed bodies which develop around such a site will disappear after X-ray applications.

The first point to consider is the healing of the chronic ulcers. Is this a proof that X-rays arrest a cancerous process? The existence of the ulceration seems to me to be a condition in which the tendency

to necrosis and death of the cells of the neoplasm is stronger than the tendency to form new epidermal tissue. It is a failure of the ordinary tendency to cicatrize which is so characteristic of the normal epidermis. When X-rays are applied and the ulceration heals the effect can be interpreted as a stimulation of the activity of the skin, and not as a selective destruction of the neoplasm. We see the very same effect in simple ulcers of the skin. X-rays are used almost indiscriminately, and with good effect, in very many morbid skin affections, and usually an effect of stimulation of its healing tendencies may be observed. I therefore do not think that we are justified in counting the healing of a cancerous ulcer as a proof of any effect of X-rays upon cancer.

In the next place, let us take the effect of X-rays in causing the disappearance of those invasions of the cutaneous lymphatics by cancer cells which are often spoken of as melon-seed bodies. We know from the writings of Sampson Handley that the lymphatics are able to destroy cancerous cells which have invaded them, and in the disappearance of the melon-seed bodies I see an instance of the effect of X-rays in stimulating the activity of the skin and of the lymphatics, rather than an instance of the destruction of cancer cells by X-rays. One might go a step further and attribute the formation of fibrous tissue in a cancer nodule, which has been recorded as a result of X-ray treatment, to a stimulation of the natural defensive powers of the tissues rather than to an injury to the cancer cells, for the formation of fibrous tissue is certainly a defensive reaction, and one which reaches a high degree of development in cases of scirrhus cancer.

It is probable that in leukæmia, another condition in which X-rays promise well at first, though disappointing in the end, the action of the rays is rather a stimulation of the natural activities of the spleen than a destructive influence. David and Desplats have supported this view that the X-rays stimulate both the hæmopoietic activity of the spleen and other organs and also the destructive effect upon the blood cells, both of which are part of the normal function of the spleen.

So far as I am aware, the evidence that X-rays can cause arrest of growth in carcinoma cells is doubtful or negative. Shattock has reported the histological examination of a growth removed after a course of X-ray treatment which seemed to have done good, and he stated that no degeneration of any kind had been induced in the cancerous epithelium, no phagocytic invasion was in progress, and on every side the growth was in an extending condition. A similar result was found in a case of my own, and I can recall a case in which after the application of radium, *secundum artem*, in the Radium Institute in Paris, an exactly

similar report was given of a small epithelioma of the tongue, which was removed in this country. No arrest of development had taken place, and the cells of the neoplasm were in a vigorously growing condition. I must except some forms of sarcoma from this statement that X-rays produce no effect upon the growth of the malignant cells. I have myself seen the complete disappearance of a sarcoma in a short time under X-ray treatment, and numbers of such cases have been recorded, but in most of these the ultimate result of the case has been the death of the patient from sarcoma, in spite of the striking local early effect of the rays. And yet there is good evidence that upon some forms of growing cells the action of X-rays is a destructive one. For instance, there is the action upon the growing cells of the testicle, of the hair-bulbs, and, though less conclusive, the effect upon gliomatous conditions in the spinal cord, if we may judge of the apparent good effect of X-ray treatment in syringomyelia, in which that treatment has produced arrest of symptoms in a number of instances.

To my mind, we have all been too much concentrated upon the treatment of the tumour. Surely none of the treatments by irradiations are so complete as the removal of the lump altogether by the surgeon's knife? And if that fails to arrest the disease, as is usually the case, it appears to follow *a fortiori* that radiations of X-rays or of radium or local ionizations or cauterizations must be even less effective; unless, indeed, the radiations are able to produce some chemical change in the juices of the body which opposes the growth of the cancer at whatever part of the body it may be. If any real good is to be done it must be by some such general chemical effect, and it seems to me to be reasonable to apply the X-rays not merely to the primary growth, but to the whole of the body of the patient, because in that way far larger chemical effects might be produced, and that without the serious disadvantages which result from over-doses of X-rays applied to a limited region. The evidence which we now need most urgently is evidence of useful chemical change in the juices of the person irradiated, and when that has been obtained we shall need to know the exact nature of the change, in the hope of learning how to intensify such chemical effects either by natural or by artificial means, that is to say, either by corresponding alterations in the X-ray technique or by purely chemical methods. The influence of Coley's fluid on sarcoma is full of significance, and the fact that its use continues to survive after years of trial seems to me also to be very suggestive.

(The discussion was adjourned until February 18.)



## Therapeutical and Pharmacological Section.

February 18, 1913.

Professor W. E. DIXON, F.R.S., President of the Section, in the Chair.

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### Discussion on the Non-operative Treatment of Malignant Disease.<sup>1</sup>

DR. ROBERT KNOX: The subject of the non-operative treatment of malignant disease is one which must greatly interest all of us who have any experience in the treatment of these conditions. Too many of our patients come to us in a condition which not only precludes operative measures, but also compels us to say we cannot do anything to help to arrest the progress of the disease. A few years ago I would have fully endorsed an opinion of this kind. At the present time I am, fortunately, in a position to at least cheer the unfortunate patient with the hope that a trial may be made in the direction of the relief of the malady. It is not yet possible to speak of curing such inoperable cases; the most we can do is to endeavour in the first place to make the condition a more tolerable one, secondly to endeavour, by such palliative measures as we possess, to transform a hopelessly inoperable condition into an operable one, and so hold out to the patient a measure of hope.

In a small percentage of cases treated by X-rays and radium, separately or combined, the tumour has been reduced to an operable size, and for a time the condition of the patient has been greatly improved. In a still smaller percentage an apparent cure has been brought about. This happens now and again; though, unfortunately, very rarely with both X-rays and radium. The rare occurrence of such reputed cures is, nevertheless, too frequent to be attributed to a spontaneous cure of the disease. Most of us who have had any

<sup>1</sup> Adjourned from January 21.



experience of cancer may have seen one, or at the most two, cases of spontaneous cure. I, personally, have seen none (though when treating desperate cases of the disease I have held grimly on to all possible lines of treatment in the vain hope that at last I might meet with the unexpected spontaneous cure; and I should have welcomed it in any form in which it might have manifested itself. I have been constantly using X-rays and radium in the treatment of malignant disease for a number of years. During that time hundreds of cases have come under my care, representing all forms of malignant disease in all its stages. The early history of X-ray treatment of cancer shows very little evidence of any permanent or even temporary results of a favourable kind.

In 1906 I recorded in the *Lancet* a case of epithelioma of the tongue with associated secondary glandular enlargement. This case received what, for that time, was a long series of radiations extending over several months. The patient died of secondary growth in the liver about fifteen months after treatment was given. The post-mortem changes were striking. The tongue growth was not treated directly, the X-ray exposures were all directed towards the enlarged glands on the right side. These glands did not diminish to any extent under treatment, nor did they enlarge after treatment was stopped. The tongue growth remained practically the same size. The lymphatic gland, which received most of the treatment, showed marked fibrosis, displacing to a large extent the gland tissue. Inside areas of the gland stained badly, both as regards the fibrous stroma and the epithelial cells; the latter were shrunken and degenerated. A small gland on the left side of the neck, which had received no direct irradiation, showed changes of a similar character, but the cancer cells were more active and plentiful, and there was also some free hæmorrhage into the substance of the growth. The growth from the base of the tongue was a squamous epithelioma, showing typical pearls and large masses and clusters of epithelial cells, which for the most part were smaller than usual. There was much round-celled infiltration present. The direct evidence of an action of X-rays upon malignant growths afforded by this case was sufficient stimulus to urge me to endeavour to obtain by improved technique a repetition of these changes in other cases.

Since those days great advance has been made in X-ray technique; and the advent of radium as a therapeutic agent threw a new light on radio-therapy. Here we have a body throwing off three types of rays, which may be utilized according to the needs of a particular case. The

Gamma-ray appeared to give good results in some cases of cancer. This ray is supposed to be analogous to X-rays, though its penetrative power is much greater than that from the hardest X-ray yet used. Workers who used radium naturally tried to produce from the X-ray tube a hard ray which would be capable of passing through metallic filters of varying thickness. Using these hard tubes with aluminium filters, and giving frequent doses, I began to get a marked improvement in the results in a number of cases. Now it is possible to reduce an apparently hopelessly inoperable cancer of the breast into one where the surgeon may interfere with some hope of success. Masses of enlarged cancerous glands have been considerably reduced in size, and later removed by operation.

In slowly growing inoperable cancer I have employed a method of treatment which may also be used in recurrence of considerable size. In several instances X-ray treatment has been pushed to a marked extent; the area of healthy tissue is protected by thick lead screens; a circular area is cut out of the screen, exposing the tumour and a margin of healthy tissue. Pastille doses of X-rays are given, at first unfiltered, later through 1 mm. of aluminium three times a week for several weeks. A marked reaction results and the tumour contracts. In one instance radium exposures were given to the central portion of the growth: 50 mgr. in a filter of  $2\frac{1}{2}$  mm. of platinum were applied for six hours. The whole of the new growth ulcerated, leaving healthy tissue behind. The resulting ulcer slowly healed, and a sound scar was obtained after about three months' treatment. This intensive form of treatment is well worth a trial in cases which do not yield to any other form of treatment. Sections removed from a portion of this growth when nearly healed showed it to be a large-celled carcinoma in small amount. The cells stained well in some groups and badly in others, while other groups were represented by granular necrotic masses. Fibrous tissue was abundant, some of it being hyaline in character. Small round inflammatory cells were distributed throughout the tumour. The area from which the portion described was removed healed over perfectly and remains well.

The following case illustrates another method of using X-rays: A woman, aged about 50, who had her left breast removed a year or two previous to X-ray treatment. The right breast was very large and hard, there was a retraction of the nipple and all the signs of a rapidly growing scirrhus of the breast. Treatment by X-rays led to a gradual shrinking of the growth. At the present date it is less than a quarter the size it was when treatment commenced; other points in the case are

increase in weight, freedom from pain, and a general improvement in health. The tumour is now in a condition where operation is possible. Frequent doses were given. The breast was divided into four areas by means of a screen and four doses given at one sitting; the tube in each instance was directed towards the centre of the tumour. The shrinkage of the tumour was obtained with practically no reaction of the skin beyond a slight reddening, and later a bronzing of the surface. In other cases the same dosage has produced marked reaction and ulceration. Aluminium filters were used, commencing with a thickness of  $\frac{1}{2}$  mm. and increasing to 2 mm. at the conclusion of the treatment.

Treatment of recurrent nodules: A large number of cases of malignant disease which come for X-ray treatment come under this class. Many of those cases are quite hopeless from any point of view so far as cure is concerned, yet the relief of pain in many cases is marked. Early cases of this type yield to repeated X-ray exposures. The routine treatment is to expose the area to X-rays at least once a week. Treatment is kept up until a marked reaction is obtained over the whole area. Should the reaction be excessive the treatment may be suspended for a month and resumed at the end of that time. Under a regime of this kind nodules disappear gradually, pain is relieved, and the patient improves in general health. After the nodules have disappeared, treatment should be continued at intervals of three weeks for at least a year, and after that should it be considered necessary.

Several cases of recurrent melon-seed bodies have cleared up for a time; repeated crops may have to be treated on the same patient. I have at least half a dozen cases under my care at present who have been treated at regular intervals for over two years. They are well and free from recurrence.

#### TREATMENT BY RADIUM.

This remedy has been extensively used during the last few years and many cases have been treated with radium alone or radium combined with X-rays. This method of using radium is important. Points on which stress should be laid are: (1) The quantity of radium used; (2) the duration of exposure; (3) the degree of filtration; (4) the condition of the patient; and (5) the type of growth, and method of treatment employed. These are all factors which influence the result.

For practical purposes, the radium is enclosed in platinum tubes which serve to protect the radium and to filter its rays. Radium is applied as follows:—

*External Applications.*—(a) To the surface of the growth and lymphatic gland areas; (b) to growths situated in mouth, pharynx, œsophagus, rectum, vagina, bladder, &c.

*Buried radium tubes* in the substance of a tumour: This method verges on the operative.

The results are not always good. A larger number of cases receive no benefit than those which do, a small percentage of the cases improve, a still smaller number show a good deal of improvement and a very small percentage appear to clear up. Types of tumour which have received benefit are: (a) Sarcoma—primary and recurrent. (b) Epithelioma: Several cases have appeared cured by superficial radium treatment. One case of epithelioma of the tonsil, already referred to, uvula and soft palate treated over eighteen months ago, cleared up and remains well. (c) A recurrent cancer of the sternum and costal cartilages has been healed, but not cured; for many months patient gained weight and showed marked improvement in the condition of the blood. (d) Endothelioma: Several cases of this kind have cleared up with radium treatment. (e) Rodent ulcer: This form is readily influenced by X-rays and radium; the difficulty is to prevent recurrence after the ulcer appears to have healed: when the disease is superficial good results may be expected.

One remarkable result was obtained by burying radium tubes into the substance of a large indurated ulcer in the groin of a patient aged 75. The whole of the ulcer broke down and gradually healed over. At the periphery a rapidly growing nodular mass appeared. This was treated by a radium tube pushed into its centre; it in turn disappeared. Later a larger mass appeared internal to the original ulcer, and a large mass was found in the left axilla. The patient died from exhaustion. The effect of the radium on the ulcer was remarkable, but the treatment did not appear to check the extension of the disease.

#### THE RELATIVE VALUE OF X-RAYS AND RADIUM.

With the great improvement in the technique of X-ray therapy, it is difficult to compare its value with that of radium, but for practical purposes, when the growth is accessible and not too deeply seated, I prefer to use the X-rays on account of the greater ease with which they can be used and the larger areas which may be treated.

Radium possesses a great advantage when tumours of the mouth, pharynx, œsophagus, rectum, vagina, uterus, or bladder, have to be treated. In such cases there is no choice—radium must be used.

#### THE ACTION OF RADIATIONS UPON TISSUES.

The action of X-rays and radium upon the malignant growth and the normal tissues is not so simple as it appears. It is not purely a caustic action, though caustic effects can readily be produced if the exposure is overdone or the filtration is not sufficient. In some growths we deliberately make use of the caustic action to produce necrosis of the mass in the hope that when the slough separates the normal tissues will fill in the resulting ulcer. This I have done in several cases. On the other hand, we see enlarged glands disappear with hardly any skin reaction. One case of recurrent sarcoma of the neck completely cleared up with merely a slight reaction of the skin surface and no permanent damage. A case of epithelioma of the tonsil involving the uvula and soft palate practically disappeared, leaving a healthy soft palate and uvula.

In addition to the direct evidence of a local action of radiations upon the cells of a new growth and its surrounding tissues, there is reason to believe that a general effect is produced upon the whole body. This is indicated by the fact that patients undergoing treatment by X-rays or radium occasionally markedly improve in general health, they gain weight, improve in colour, and when the blood is examined an improvement is seen. As an illustration of this beneficial effect I mention the following case, which has recently come to my notice, where treatment of a large, foul ulcerated carcinoma of the breast was followed by a marked improvement in a foul vaginal discharge from which the patient suffered. While treating growths of the breast, it is not uncommon to find glands in the axilla and other parts diminish in size. This is also observed when cases of sarcoma, lymphadenoma and other diseases are treated. Whether this is the result of a general stimulation or an auto-vaccination is a point which has yet to be determined. Experimental evidence is forthcoming which goes to show that cancer which has been treated with X-rays or radium does not grow so readily when inoculated into mice as growth which has not had such treatment. It is extremely probable that radiations of X-rays, radium, and similar agents do exercise a general as well as a local effect upon living organisms. The general effect may be quite as useful as the local, and if it has any

value at all it would be extremely useful to bear in mind, because one need not then be limited in area of exposure. After local treatment has been pushed to its limit the treatment may be continued in other parts of the body.

The following observations made on patients undergoing treatment for malignant disease may throw some light on the problem which has been engaging our attention for so long. In the course of treatment of cases of leukaemia the fact has been observed that marked changes can be induced in the blood by radiations; a diminution in the number of white blood corpuscles relative and absolute can be readily produced. The changes are obtained when the splenic area is irradiated, as has most generally been the case in treating this disease. The same changes may be brought about when other parts of the body are subjected to treatment; thus the irradiations of the ends of the long bones or other areas of the abdomen result in a change in the percentage of blood cells and a reduction in the size of the spleen. Observations such as these lead us to infer that the beneficial effects of X-rays on certain cases of this disease may be due to a general as well as to a local action. Further, it has been observed during the local treatment of carcinoma of the breast, that glands at a distance which have not received any direct treatment have slowly diminished in size. It has also been noticed during the treatment of such diseases as tubercle, lymphadenoma and sarcoma, that while the local condition has improved as a result of direct treatment the more distant glands have also diminished.

I have for several years been making observations on blood changes induced in patients undergoing treatment by radiations. At the commencement of these observations the whole attention was directed to the white blood cells, which were observed to vary considerably at different stages of the disease according to the accompanying infection, and also as a result of destructive changes occurring in the tumour and surrounding tissues. More recently my attention has been directed to the behaviour of the red blood corpuscles under similar conditions. As an outcome of these observations we can state that in cases where the percentage of red blood cells is normal or over, and the hæmoglobin is nearly 100 per cent., the response to treatment is more rapid and lasting than when, as is too frequently the case in advanced stages of malignant disease, the percentage of red cells is much below normal. In several patients whose response to X-ray and radium treatment has been rapid and marked, the percentage of red cells has been well over the normal. One case recorded well over 8,000,000, and the hæmoglobin



colour index stood at 100 per cent. Nearly every case examined which showed a normal or plus normal condition of the red blood cells responded promptly to X-ray treatment.

In view of the excellent work done on secondary radiations of metals by Barkla, Sadler, Russ, Philips, Whiddington, and others, the most likely explanation of this remarkable response in these cases is that in the blood-stream there exists a material, or materials, which when bombarded by the radiations of X-rays or radium throw off secondary radiations which in some way act on the normal and abnormal tissue, stimulating the former and in some instances damaging the latter and leading to a diminution in the size of the tumour. The most likely constituent of the red cells is hæmoglobin, a compound of iron. The latter metal is known to give off secondary radiations when exposed to X-rays. It is interesting to note that iron stands high in the list of metals which give off secondary radiations when struck by X-rays. These radiations are independent of the chemical combination of the metals and only depend upon the quantity of the metal present. It must be borne in mind that metals require a particular hardness of X-ray to enable them to emit the characteristic secondary radiations peculiar to them. This may in part account for the marked degree of action produced in cases which have a high percentage of hæmoglobin. It also throws some light on the cases which have failed to respond; possibly the particular quality of X-ray employed has not been the proper one, or the exposure may not have been long enough. In my own experience the best results have been obtained when using the hardest X-ray possible combined with aluminium filters.

The hard Beta-rays and the Gamma-rays from radium appear to exercise a marked influence on some cases of cancer. The duration and frequency of the exposures also play an important part in the results. At present experience alone can show us how and when to repeat the radiations.

When the secondary radiation value of the constituents of a malignant growth and of the blood and lymph and the substances they contain are known, and when improvements in X-ray tubes and control apparatus enable us to select the ray which will, when it strikes upon, say, the iron in the blood, cause it to emit its secondary radiation, we may hope to produce a reaction in and around the growth which should materially help us in treatment. Then we may hope for marked improvement in results. It is probable that we have here also an explanation of the changes which may be induced in the more distant



parts: the blood which receives local treatment in its passage through the growth and surrounding tissues is acted upon by these radiations, and the effects produced on the cells in the local growth are carried on to the other parts of the body and exercise a stimulating effect on tissue metabolism which may result in changes in those parts. The suggestion is, I think, one well worth careful investigation and consideration, for here we possess an excellent vehicle by means of which we can obtain secondary reactions from direct radiation upon particular parts. The obvious inference is that in all cases of malignant disease we should endeavour to keep the red blood corpuscles up to or above normal in numbers and colour value, by giving the patient iron and other drugs which are known to exercise a tonic effect, while we bombard the local condition with regular doses of radiations. The radiations should be of a quality which is known to produce the secondary effects upon the iron in the blood. The treatment of a malignant growth must therefore be general as well as local.

The general treatment consists of a suitable diet, plenty of fresh air and iron tonics—the latter in excess if the patient is tolerant. It should be pointed out that rest in bed during treatment should in some cases be insisted upon. The local treatment should consist of, firstly, such measures as will induce a liberal flow of blood to the part: (1) Brush high-frequency discharges are very useful for this purpose and should be given just before or at the same time as the X-ray treatment; (2) the mercury vapour lamp also induces an increased blood flow.

The X-ray or radium exposures should be of sufficient duration to induce and keep up in the tissues a moderate degree of reaction. It has been observed that improvement hardly ever takes place until this degree of action is produced. In severe cases the reaction may require to be marked. Under treatment of this kind recurrent nodules of all sizes and degree frequently disappear, large tumours become smaller and in some instances are rendered operable.

I feel convinced that if the cure of malignant disease is ever to come from treatment by physical methods it will be from the introduction into the blood- or lymph-stream of a substance or compound which, while innocuous in itself, is capable, when stimulated locally, of giving off radiations which can exercise a degree of action upon morbid processes. Such a substance would be constantly circulating through the growth and when acted upon locally by X-rays or radium would give off its curative properties in a continuous manner according to the degree of radiation employed.

It is also possible that the blood serum may contain substances which give off secondary radiations which alter the composition of the serum. A great deal of work has been done in this direction. Future research in the investigation of physical phenomena should be directed on lines which are likely to throw light on secondary radiations in the tissues themselves. By a combined attack from the physical and clinical aspects, we may hope in the near future to make a marked improvement in our methods of treatment by radiations which should result in material benefit to our patients suffering from malignant disease.

In conclusion, I may frankly state that until a better and surer remedy comes into our hands, we should diligently pursue the treatment of inoperable disease with X-rays and radium in the certainty that we can, at all events, relieve a percentage of our cases, render operable a small percentage, and in a larger percentage afford marked relief of symptoms and a diminution in the size of the growth.

Mr. CECIL ROWNTREE: Of the papers hitherto read, the majority have been concerned with methods of treatment which in the main are directed to the actual cure of cancer. However successful these methods have been, the fact remains that there are still very many cases of advanced cancer in which the progress of the disease is not checked; and yet others where, after a temporary improvement attributable to some special treatment, the growth again extends. In fact, in all patients who *die* of cancer, a time comes when the application of X-rays, radium, or diathermy, or such procedures as the palliative removal of a growth, or the occlusion of its blood supply, are no longer possible.

As I have had the opportunity of observing many cases of malignant disease throughout their course, I should like to refer to what I believe to be the most valuable of the various non-operative methods used in the treatment of the symptoms of cancer as distinct from the treatment of cancer itself. I take it that the cardinal symptoms of cancer are pain, ulceration, discharge, and obstruction of either the alimentary, urinary, or respiratory tracts. These obstructions, however, cannot be treated by any means other than operation, and may therefore be omitted. We are left with pain, ulceration, and discharge as the symptoms of chief importance and most frequent occurrence.

*Pain.*—The pain of cancer may be due either to the direct involvement of terminal nerves by the primary growth, or to pressure upon

nerve-trunks or nerve-roots by the growth or by its metastases. There is another common kind of pain, however, the nature of which is, I think, sometimes overlooked; and that is the pain produced by the presence of growth in any of those structures which undergo peristaltic or similar movement: that is to say, the intestine, the ureter, the bladder, and the pharynx. In each of these cases the growth acts partly, of course, as a foreign body; but also owing to its infiltration between the muscular fibres of the affected organ, it blocks the passage of peristaltic waves, and so interferes with the motor mechanism of the part, setting up violent, irregular, and painful contractions which occasion the utmost misery.

The most common and the most valuable method of relieving pain is, of course, the administration of sedative drugs, and of these morphia is unquestionably the most effective; but, unfortunately, the pain of cancer is not a temporary thing, and owing to the systemic disturbance that the long-continued use of morphia occasions, it should never be given so long as the pain can be relieved by other means, but should be reserved for the last stages of the disease or for those few cases in which relief can be obtained in no other way. Phenacetin is a drug of the utmost value which is used extensively at the Cancer Hospital. In doses of 10 gr. every six hours, combined with 5 gr. of caffeine citrate, it does all that is necessary in a large proportion of the cases. A great advantage is the fact that no progressive increase of dose becomes necessary. When phenacetin is not effective, or when it produces cardiac depression, aspirin in similar doses is found to be a useful variant.

There are scores of other drugs, of course, all useful in their place, but none with the wide application of those I have mentioned. One of these—viz., omnopon—will be found of great use in cases of severe nerve-trunk or nerve-root pain where heavy doses of morphia would otherwise be necessary. It produces slight drowsiness and freedom from pain, but without stunning the patient as morphia does, and without leading to any unpleasant after-effects. A small dose administered hypodermically gives relief lasting sixteen to twenty hours.

In a few cases of ulcerated growth the surface of the ulcer is so sensitive—probably owing to exposed nerve-filaments—that the mere change of dressing causes great pain. Large rodent ulcers and extensively ulcerated breasts are the kind of case I have in mind; and it is possible to relieve them by painting the surface with a dilute solution of adrenalin and eucaine.

I now turn to the non-operative methods of destroying the physiological continuity of the implicated nerve or nerves. Intraneural injection of alcohol has not had the wide application in the treatment of malignant disease that at first sight seemed possible, owing to the fact that cancer, unlike neuralgia, is not usually confined to the area of any one nerve or group of nerves, and consequently it is not easy to pick out the nerve particularly involved. However, in certain cases it has been utilized with great success, particularly in advanced cases of cancer of the tongue where the lesion is confined to the area of distribution of the third division to the fifth nerve. In these cases the injection of 20 minims of 80 per cent. alcohol into the foramen ovale has been followed by very satisfactory results, and the destruction of the conductivity of the nerve is, of course, sufficiently permanent to last the lifetime of the patient. Another method of blocking nerve conduction that has been utilized in cases of sarcoma of the pelvis or cancer of the uterus and rectum is the injection of small doses of stovaine or some similar substance into the spinal theca and the production of a limited degree of spinal anaesthesia. This method of treatment is still in its experimental stage, and further experience is necessary before it will be possible to define its value.

In reference to the injection of alcohol into the Gasserian ganglion, it is perhaps not quite fair of me to include it among non-operative measures, because although it is possible to do it without an anaesthetic, yet I do not like doing it. But, unfortunately, in some of these advanced tongue cases, the administration of an anaesthetic is a very difficult and hazardous proceeding.

I need not say anything about the treatment of pain by X-rays or radium, as that has already been dealt with, but I do not wish to appear to minimize their importance by leaving them out; and I therefore just mention the great value of X-rays, and particularly of radium, in the relief of pain.

*Ulceration.*—Ulceration is almost certain in all malignant growths, and directly ulceration has occurred, hæmorrhage, septic absorption and discharge inevitably follow. I think one can sometimes do a little to delay ulceration by painting collodion over the thinned skin covering the primary growth or its secondary deposits, and by avoiding the application of warmth or moisture; but one only gains a few days by these preventive measures, except in instances where extensive breaking down has taken place before the skin itself is much involved; and I am thinking now more particularly of those common cases in which malign-

nant glands in the neck, axilla, or groin suddenly enlarge and liquefy : presumably as the result of a secondary infection. In these cases great relief of pain, much diminution of the swelling, and considerable delay in the destruction of the skin may be obtained by thrusting a hypodermic needle obliquely into each cavity and withdrawing as much of the fluid contents as one can. When ulceration is established, all that we can do is to endeavour to check its progress by keeping the surface clean by the use of some form of local application. There are, of course, many instances in which it is impossible to use any of the special methods, such as diathermy, and in these cases, in order to reduce discharge and fœtor, we must simply fall back on the ordinary antiseptic washes copiously and frequently applied. I think the solution most generally employed is sanitas. It can be used in the mouth, the vagina, the rectum, or, indeed, in any part of the body, and it has the great advantage of possessing a pleasant smell which assists in concealing the offensive nature of the growth. I never use antiseptic lotions that do not serve this double purpose. Perchloride of mercury, biniodide of mercury, &c., are, I think, much inferior to the coal-tar preparations, such as sanitas, cyllin, and lysol. As to the actual dressing of the ulcer, I know nothing better than peroxide of hydrogen of the ten-volume strength. This penetrates all the cracks and crevices, searches out dead organic material, and cleans up with great rapidity. It occasionally causes pain, and must then be diluted. The usual warm antiseptic compress, so useful in the ordinary sloughing wound because it stimulates repair, is, I believe, a mistake in these cases, because there is no repair to be stimulated, and the moist heat favours bacterial growth. The application of peroxide, followed by a dry dressing where practicable, gives better results.

Acetone has been used in recent years for the purpose of dehydrating and hardening the surface of a growth and so diminishing bacterial activity ; but unfortunately the application of acetone is often very painful, and consequently its use is limited. For some time I attempted to obtain a somewhat similar effect by the use of a dilute solution of aluminium acetate. The results, however, were not encouraging, and I now no longer use it.

*The Treatment of Discharge.*—A great deal of the discharge is, of course, the direct result of ulceration, and is simply an index of the amount of tissue destruction or of the degree of bacterial activity. But in many cases discharge is of a different origin. It is produced by hyperactivity of mucous glands in the immediate neighbourhood of the

growth. The positions in which this is particularly seen are the rectum, œsophagus, and pharynx. In the case of cancer of the pharynx and œsophagus, the constant regurgitation of large quantities of frothy mucus is particularly unpleasant and disturbing, sleep being interfered with to a very marked extent. In these cases very great relief may be obtained by the administration of tincture of belladonna in small but frequently repeated doses. There can be no doubt as to the diminution of secretion. The treatment of discharge by bacterial vaccines is an important matter to which I should like to refer, although scarcely competent to do so. But I do think that in such cases as cancer of the cervix, where patients rarely die of cancer but of septic processes arising from the growth, the possibilities of affording some relief by vaccine therapy have not been sufficiently considered by practical bacteriologists. It is true that the number of organisms present is legion, but surely systematic investigation of a series of cases might not unreasonably be expected to result in the isolation of one or more what may be called master organisms from which vaccines could be prepared. Something of the kind is being done in early cases of uterine cancer as a prophylactic against post-operative infection; but in these early cases, of course, the vaginal flora are neither so complex nor so numerous.

So much for some of the measures that may be adopted for the relief of the symptoms of inoperable cancer.

I should now like to refer to those forms of treatment whose primary object is not the mere relief of symptoms, but the cure of the disease. Of these I put Coley's fluid first. We are probably all familiar with Dr. Coley's work, and we know that he claims to have cured about 10 per cent. of his cases of sarcoma of bone by injection of the mixed toxins of *Bacillus prodigiosus* and *Streptococcus pyogenes*. Those who have met Dr. Coley or who heard him lecture at the Surgical Section cannot fail to have been much impressed by his enthusiasm and scientific spirit. But the fact remains that the results obtained by Dr. Coley have not been repeated in this country, nor do they appear to have been obtained by those few American surgeons with whom I have had the opportunity of discussing the question.

I have used Coley's fluid in a good many cases, and at one time I thought and hoped that the reason why satisfactory results were not being obtained in this country was because our technique was wrong and our material perhaps unsuitable, for there are, or there were, wide variations in the potency of the different preparations of Coley's fluid on the English market. But last year it happened that I had under my



care two cases of sarcoma of bone while Dr. Coley was in London. He very kindly saw them for me, sketched out the line of treatment, and very generously kept me supplied with toxins prepared in his own laboratory. Both cases were treated assiduously for a long period. In neither was there any beneficial result, and in one of them I am quite certain that injection of the fluid directly into the tumour was coincident with rapid increase in its rate of growth, which diminished again when the injections were made elsewhere. Both these patients are now dead, but, in fairness to Dr. Coley, I must explain that they were both advanced cases: one, recurrent periosteal sarcoma of the femur; the other, sarcoma of the ilium. None the less, it is true that a few cases of sarcoma here in London have been benefited or apparently cured by Coley's fluid; and I am personally familiar with some of them, although the only case of apparent cure I have seen was that shown by Major Spencer at the Clinical Section some two or three years ago.

Therefore, in spite of my disappointing results up to date, I still believe it to be our duty to treat all cases of inoperable sarcoma of bone by this means, combined or not with such other methods as the implantation of radium.

A difficulty met with in carrying out a systematic course of treatment is the disinclination of the patient to face the malaise and discomfort occasioned by the daily injections, and in some cases the systemic disturbance is so great as to render it impossible to continue, at any rate without diminishing the amount or frequency of the dose of toxins.

Dr. N. S. FINZI: I propose to deal with the treatment of malignant disease by the use of radium or X-rays, and I may say at once that both of these have their own separate sphere of usefulness, though the principles of treatment by them are very much the same. We have during this discussion had a very pessimistic account of the outlook of X-rays from Dr. Lewis Jones. I do not agree with the views he has expressed, though they coincide with what was my opinion before I adopted the methods of massive doses and filtered radiations. These methods completely altered my results with X-rays and made them a much more effective agent than they used to be. The principle of the action both of radium and X-rays is that a dose of radiations which will do no harm to healthy tissue is sufficient to destroy the cells of most neoplasms. I do not suppose that it is a property of the rays themselves, but I expect that it is some property



of the cell that renders it more susceptible to their action than healthy cells; this, I think, one is quite justified in describing as selective action, especially as it is exerted much more on some types of growth than on others. This selective action is also more marked in the case of filtered rays of radium than in the case of filtered X-rays; for instance, I have several times found that a growth which showed no response to X-rays has been considerably improved, or has even disappeared, with radium treatment; or if the growth has responded to X-rays it has responded much more readily to radium rays. The selective action is sometimes so marked that it is possible to get rid of tumours without injuring the skin over them.

The use of radiations being confined, apart from prophylaxis, to inoperable cases, the most one should expect is to obtain some relief; nevertheless in a number of cases now have I seen complete local disappearance of a proved malignant growth and, though some of these patients have subsequently died from metastases or intercurrent disease, there are several of them still living. The case I have seen which has been longest free from disease was one of lympho-sarcoma of both sides of the neck and mediastinum, which was treated by Kienböck, of Vienna, about eight years ago. All signs of the disease were got rid of, though of course the scar in the mediastinum has altered the position of the contents of the chest considerably. This growth was proved microscopically to be a lympho-sarcoma. Some time last year he developed a sarcoma of a different character in the jaw and this was removed surgically; there has, however, been no sign of recurrence of the original disease. Another case which came under my notice was an osteo-sarcoma of the iliac bone, proved histologically, which was treated in Germany and which recurred five years later. I treated the recurrence and this again disappeared, but unfortunately I lost sight of the patient about a year later, as he probably returned to Germany. The chief factors which influence us in deciding whether to use X-rays or radium are as follows. If the growth is localized it is better to use radium, but if there are chances of metastases over, or if the growth covers, a very large area, it is difficult to get a sufficient dose to the deeper parts with the amount of radium available at present, and the large area to be treated takes a very long time to cover, during which the use of the radium is limited to the one patient. Thus in a recurrent carcinoma of the breast where we feel fairly certain that there is recurrence in the mediastinum and possibly in the liver, in the

supraclavicular glands, and so on, it is better to use X-rays, notwithstanding the fact that they have a lesser selective power. If there is an ulcer, however, this may be treated with radium, while for the rest of the area X-rays are used. If a growth is superficial where it can be got at easily with either radium or X-rays, the former will be better. Where it is possible to insert radium tubes into the substance of a tumour, especially when it is a type which reacts readily, it is a great advantage to do this, as the rays act in every direction, and by regulating the dose the central part may be considerably overdosed while the growing edge receives just sufficient to destroy it. In using this agent as a prophylactic also it will be found useful to leave radium tubes in the site of removal of a growth for a few hours; here, of course, only giving a dose which will not harm healthy tissues, otherwise a sinus would remain. When, however, an operation wound has been closed up the area is generally too extensive for satisfactory radium treatment, and X-rays should be employed.

Prophylactic treatment is based on the fact that the earlier a growth is obtained, that is, the less advanced, the better will it react compared to a later one of the same type, so that if after an operation the chance remains of a few cells having been left behind these will be much more readily destroyed than if we wait for a recurrence. The principle of treatment by both X-rays and radium will be the same; they are as follows:—

- (1) Use maximal doses.
- (2) Repeat as frequently as is safe.
- (3) Use sufficient filtration.
- (4) Treat thoroughly not only the growth itself but any region in which it is likely a metastasis might exist.
- (5) Continue the treatment after all traces of disease seem to have disappeared.

The maximal dose of X-rays filtered through 2 mm. of aluminium that I care to use on a healthy skin is  $1\frac{1}{2}$  Sabouraud dose, measured, of course, after the rays have passed the filter, and I find that this can be repeated in most patients once a fortnight. When applying the rays to a malignant ulcer very much larger doses may be used, but to obtain the best effects filtration should still be employed. The filtration I usually employ is 1 mm. to 3 mm. of aluminium for X-rays, and I would emphasize the fact that I use this for superficial growths as well as for deep ones, on the ground that the selective action is

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greater and less sloughing and inflammation are produced, and a greater absorption of the neoplasm than would be the case with unfiltered rays. I consider it an advantage to give the dose in the minimum possible time, as apart from the patient's convenience I believe the results to be more effective. With radium also it is necessary to give the dose in a minimum time, therefore the largest quantities possible should be used. For malignant disease a filter is always advisable, and it is best not to use less than 1 mm. of lead: the amount I usually employ myself is 2 mm. of platinum, which is equivalent to about  $3\frac{1}{2}$  mm. of lead. The platinum is used in order to get the apparatus into smaller space. It is absolutely essential to treat the whole of the infected area and any point at which in a similar case one might expect metastases. Thus in a carcinoma of the breast one treats the axilla, the supraclavicular region and the mediastinum, even if no growth in these parts can be discovered; similarly, in a malignant form of sarcoma one would treat the lungs with X-rays on account of the frequency of secondary deposits in them.

When all sign of growth has apparently disappeared it has in several cases been proved that a few cells may remain, therefore it is necessary to continue the treatment for some time, and my usual plan with radium is to give at least two full doses subsequently and with X-rays about six.

With regard to what Dr. Herschell has told us about colloid copper I am extremely interested. I understood him to say that the copper was actually deposited in the growth; if this is really the case the employment of X-rays or radium on such a growth will cause the copper to give out a large amount of secondary radiations and lead to the destruction of anything in the vicinity of the copper compound which exists in the tissue. If this method really picks out every growth cell it holds out very great prospects of success by combining the two treatments.

In conclusion, I may say that from the point of view of treatment by radiations inoperable cancer has a far better outlook than it had a few years ago, and that occasionally when we only expect improvement we have obtained such success as will enable us to hope for and expect a cure.

Mr. IREDELL said that probably all present would agree that it was safe, in the long run, in the case of cancer, to have it removed surgically, if that were possible; and, if not, to try treatment by X-rays or radium.

He agreed that a number of cases had been treated effectively with X-rays and radium, but even those cases in which there was a prospect of success by that means were exceedingly small compared with the number of people who died every year from the disease. The figures quoted by one of the speakers at the former meeting showed that, so far, none of the forms of treatment had had any real effect on the mortality attributable to this disease. The chief qualifications for success in treatment of a case of cancer with either X-rays or radium were, first and foremost, accessibility. The next was that the growth should be small; the third, that the patient should be thin; the fourth, that it should be slow-growing. Lastly he would mention an indefinable quality which might be called the presence or absence of response to treatment.

The first two qualifications were most frequently found in cases of breast cancer, chiefly in the matter of recurrent nodules. These recurrences took place most frequently in the scar, the sternum, the ribs, the supraclavicular region, and the axillæ, the last in some cases causing a swollen arm. It was unusual to find recurrences in the spine, the brain, the liver, without there having been such also in one of the situations just mentioned. It followed as a corollary, though he said it with hesitation, that if the recurrences in these cases were efficiently treated, it was possibly the case that recurrences in the other situations might be avoided. It was in these cases that he regarded both X-rays and radium as useful. But he had also found those means useful in cases of inoperable cancer of the breast, and in primary growths or recurrences of lip, rectum, œsophagus, &c. It was no doubt occasionally useful in cases of disease in other situations. Comparing X-rays with radium, X-rays were more easily obtained and used, and had the additional advantage that a large area could be treated at the same time; and from that point of view they were useful as a prophylactic. Physically, the rays given off by X-rays and radium were of the same nature; but apart from the physical properties, it seemed to him in regard to human cancer that a given tumour had very much more prospect of being cured by radium than by X-rays. That he considered to be due to two factors: first, that in a given time, radium, in moderate doses—i.e., 10 or 20 mgr.—did more good to a growth than did X-rays, and secondly—and this was a property of even greater importance—that while X-rays could be applied for, at most, one or two hours to any patient, radium, if properly protected with lead, could be used continuously for many days, with corresponding benefit. He had found cases which did not respond to X-rays clear up with the application of

radium. He had not, however, known a case which did not clear up under radium do so on the application of X-rays. There could be no doubt that the large majority of the cases of the disease which were treated with radium were failures in the end—i.e., death occurred from cancer, either in the situation which had been treated or elsewhere. And the causes of this failure could be placed under two heads: (1) That there was a secondary deposit which had not been known at the time, or which had arisen in an inaccessible situation; (2) failure of the radium to influence the growth itself.

In his efforts to prevent the spread of cancer, he had given radium in solution for inhalation, radium salts in solution, and in the form of a powder. But in only one case did it seem to have any effect, and that was in a growth of the lung—a good situation, inasmuch as radium when given internally was partly excreted by the lungs. He gave a gramme of radium activity 250, divided into ninety doses, giving three doses a day. It was followed by a definite increase in the cough for twenty-four to thirty-six hours afterwards. He was, however, unable to find any definite signs of improvement after it. In several other cases, in some of which radium was given in different forms for six months, there was no influence on the progress of the growth. This failure of X-rays and radium to cure the growth was of interest, and a typical case might be instructive. It was that of a patient in whom, as in the others, the diagnosis was arrived at microscopically; and the growth was carcinoma of the rectum. It was treated with  $22\frac{1}{2}$  mgr. of pure radium, at intervals of a month, each application for forty-eight hours, with the usual amount of protection by lead and other wrappings. She was a lady aged 37. The result of the first few applications was most successful, inasmuch as the bleeding, discharge, and necessity of straining were stopped; also the raised edge of the ulcer became flatter, the ulcer smaller, and the walls were reduced in prominence. For some months this improvement continued, then became stationary, and finally there was a recommencement of the bleeding and discharge. Six months later it was decided to do colotomy. This was typical of many cases one had unfortunately to see; and the question naturally arose as to whether anything could be done to continue the beneficial effects of the radium. Was it, by increasing the amount of radium, possible to do much good? In the case of one patient, a woman who had had one breast removed, and who had a recurrence, a small growth occurred in the other breast. He had the opportunity of using 90 mgr. of radium, but while at first the growth diminished, finally the radium

lost all its effect, and the growth increased in size, just as the other did. In another case, a small growth in the cheek was treated by radium. The patient not noticing much improvement, she went to another doctor, who treated the site with several hundred milligrammes, but with apparently no better result, because the growth was afterwards removed, though unsuccessfully as regards recurrence, and the patient ultimately died of the disease. This effect had been confirmed by Smith, in his work on mice cancer; he used varying amounts of radium, varying between 1 and 8 mgr. He found that while ulceration was much more quickly produced with 8 mgr., he was unable to note any marked change, if any at all, in the way the various growths responded to the various amounts of the salt.

While he (the speaker) did not think it would be fair to compare, in this matter, the relative weights of mice and men, in regard to the amounts of radium employed, it was interesting to note that probably 8 mgr. in the mouse would correspond to some thousands of milligrammes in man. He believed it really meant that the reason radium failed in curing cancer was not so much a fault in the radium as a fault in the cancer cell—i.e., it got accustomed to its new environment and resumed its activity of growth, ignoring the influence of the Gamma-rays. That was what had been noticed by embryologists with regard to embryological cells, which, as was well known, were closely allied to cancer cells.

Dr. ALEXANDER HAIG: For years I have been pointing out that uric acid is a cause of very widespread injury to the tissues of the body, and might in this way take part in the causation of malignant disease, which notoriously affects parts subject to chronic injury—e.g., fractures, old wounds, &c. More recently I have pointed out the many and important relationships between gout, rheumatism, and malignant disease—the way in which they all three affect certain parts and tissues and avoid certain other parts. Some of these effects are very remarkable and point rather strongly to identity of causation.<sup>1</sup> Then Mr. H. C. Ross, and more recently Mr. H. C. Ross and Dr. J. W. Cropper have shown that several substances closely related to uric acid, and which are certainly present in the body, as forerunners of uric acid, caused cell proliferation. They have called these substances “auxetics,”

<sup>1</sup> See *Med. Record*, N.Y., 1912, lxxxii, p. 645.



and their work has been confirmed by others, especially in relation to the production of malignant disease by gas-tar. According to these investigators, for the production of malignant disease you require the presence of an "auxetic" such as xanthin, which is present in the blood in gout, and an "augmentor" such as cholin or cadaverin formed from the decomposing products of tissue destruction. Thus, when gouty inflammation produces tissue destruction in a part of the body (uterus, larynx, &c.) which cannot be kept clean, you have all the conditions necessary for the production of malignant growth. Paraffin and X-ray cancers may be cited as instances of this sequence. Thus, my conclusions arrived at long ago from physiological and pathological chemistry have been confirmed up to the hilt by the work of others.

There is, again, no practical doubt that the diet which prevents gout, prevents malignant disease. This is perhaps best seen in the case of religious communities, who may be living among a people having a high cancer death-rate; but owing to their frugal fare and simple, laborious lives, such community may have a very low cancer incidence. Dr. Kellogg, of the Battle Creek Sanitarium, has pointed out that the same thing is seen in the case of the large resident population of the Sanitarium who live practically on the uric-acid-free diet. He has never, in some forty years' experience, seen malignant disease in any of the staff who have been on reformed diet for two years. Personally I have no doubt that the diet which prevents both gout and malignant disease will, in some cases, also cure malignant disease. It will be most likely to do this in the case of slow-growing disease where it gets time to act.

I have also seen a considerable number of cases in which diet has apparently prevented recurrence of malignant growth after operation, though in such cases it is difficult to be sure that *post* is *propter*. I have also seen a few cases in which diet appeared to cure, and a considerable number of more or less similar cases have been reported by others, though no complete explanations have yet been given of the fact. I believe that if such cases are carefully investigated, it will be found that the cure has occurred in relation to an increased solubility of uric acid in the body. I believe that diet, when it does cure, acts both by stopping fresh introduction of uric acid and by dissolving out what is already there. Further, I have shown<sup>1</sup> that life may be divided

<sup>1</sup> "Uric Acid," 7th ed., p. 236.



into four stages, in two of which uric acid is retained in the body, and in two of which it is excreted in excess. During the retention stage gout or rheumatism and cancer will flourish. During the excretion stage all three will more or less markedly retrogress or disappear. Thus the very uric acid which causes the rheumatism of childhood (first retention stage) causes also the anæmia of 17 to 25 (first collæmic stage); the rheumatism diminishing as the anæmia increases. A similar change of solubility takes place at the other end of life from 55 onwards, and this may account for the slow growth or retrogression not infrequently seen in malignant disease above this age.

Mr. Roger Williams<sup>1</sup> shows that there is a great rise in its incidence at and above the age of 25, when, as I remark, the first collæmic stage gives place to the second or great retentive stage. He says (*loc. cit.*, p. 318): "Cancer begins to be frequent in both sexes after the twenty-fifth year." He points out on p. 319 that there is a marked drop in mammary cancer after 55, when the second retentive stage gives place to the second collæmic stage; thus the incidence of mammary cancer at 60 is less than half what it is at 50. He further shows (*loc. cit.*, p. 320) that the incidence of cancer in the eighth and ninth decades is only about one-fourth part of what it is in the fifth decade, this latter being the time when, as I have shown, the quantity of uric acid retained in the body reaches its highest point. These facts can also be seen in all the reports of the Registrar-General and are well shown in that for 1910.

Cancer, in fact, like gout and rheumatism, is a disease of the vigorous and of the retention stages of life. In cases that appear to have retrogressed spontaneously, a change similar to that of a collæmic stage has been produced either by age, by accidental injury, or by a change of diet. I believe that in all such cases a solution and removal of uric acid will be found to have been in progress during the retrogression. A poor person living in the rural districts of Ireland, and eating much potato, may be free from rheumatism, but on moving to a large town and eating much meat and less potato, may get rheumatism badly. A similar change of diet in the opposite direction about 55 or later may make the difference between a progressing and a retrogressing growth. One uterine case I saw four years ago was thought to be malignant by those who sent it to me, but was not proved so by microscopic examination. I said, "If the tumour increases, operate, if not leave

<sup>1</sup> "Natural History of Cancer," chap. xv.

it alone and keep to diet." It was not operated on, and now it has almost disappeared and gives no anxiety. Another uterine case, quite inoperable and proved by microscopic examination to be malignant, retrogressed on nuts and fruit. The patient died some four years later as the result of an accident, having long ceased to think about the tumour. The diet in this case was very strict, nuts and fruit only. The patient was rich and could afford this diet, but potatoes and nuts would be cheaper, and I believe equally good as a diet for the poor. I believe that this last case and some reported by others are not accidental, but results of the solution and removal of uric acid by an alkaline diet, together with the cessation of all introduction of fresh uric acid. The diet here acts in producing cure just as the diet of Battle Creek does in prevention. I think that free use of potato, with its solvent salts of potash, accounts for much of the lower cancer death-rate in rural parts of Ireland.

All these facts point in one direction, and agree in showing that the conditions which cause and cure gout and rheumatism have also a most important influence on the incidence and course of malignant disease. Malignant disease (like gout) affects the acid parts of the body<sup>1</sup> as well as the retention stages of life. As we have considerable power over the arthritis, I believe we shall soon be able to demonstrate some considerable power of control over malignant disease also.

To sum up as regards treatment, we must stop at once all fresh introduction of uric acid, we must make conditions as favourable as possible for its solution and removal. The nut and fruit diet, mentioned above, fulfils both these conditions, and its action will be aided by warmth, hindered by cold (and malignant disease is especially rife in the cold regions of the world), hindered by retentives of, aided by solvents of, uric acid, especially heat and the alkalies. A milk, rice and curd diet can be used as a stepping-stone to that of nuts and fruit.

It is now quite easy to cure bronchitis by alkali in two or three days, thus stopping a very obvious and violent injury of the bronchial tissues.<sup>2</sup> I believe malignant disease will often react to similar treatment, just as chronic gout does, in two or three months' time. Those who live uric acid free get neither bronchitis nor malignant disease. For years past those surgeons who have had to operate on patients on the uric-acid-free diet have been struck by the entire absence of inflammatory reaction,

<sup>1</sup> See *Med. Record*, October, 1912.

<sup>2</sup> See *Brit. Med. Journ.*, 1908, i, p. 1100.

and the rapid healing of wounds, and some now put their patients on this diet for a longer or shorter time before operation.

We can now see, thanks to the work of Ross and Cropper, that it is precisely the conditions which favour this rapid healing of wounds that will prevent auxetics and augmentors from producing malignant disease. Obviously, in any treatment we must avoid auxetics and any causes which, by producing local injury, tend to produce gout and rheumatism by precipitating the urates. Our whole object must be to remove the urates from the tissues and to keep them out.

It seems, then, that gout is but a stage in the production of malignant disease, and that this accounts for all the clinical phenomena mentioned above. It accounts also for the difficulty in diagnosing between a gouty and a malignant arthritis, for one stage is here passing into the other under our very eyes. Both stages can rightly be called the rich man's disease.<sup>1</sup> Dr. Berkart, who pointed out in the *Lancet*<sup>2</sup> that a gouty tophus had a structure not unlike that of a sarcoma, had perhaps arrived on the verge of an important discovery by a different route.

For the notes of the following interesting and suggestive case I am indebted to my friend, Dr. Charles Gayford, of Bank Chambers, Strand, who kindly permits me to use them to-day: I. R., chemist, aged 46, married. Robust health from childhood. Mother died of carcinoma, aged 59. Doubtful history of specific disease. 1903: Suffered from sudden loss of voice and has been husky ever since. Has taken much liq. hyd. perchlor. and pot. iod. July, 1905: Seen by Dr. Gayford, who noted that there was a well-marked gouty pharyngitis. He had a short, dry cough, some scanty expectoration in the morning, and a slightly enlarged gland on the left side of the neck. His expectoration showed large numbers of uric acid crystals and gave a murexid test. Many subsequent samples of expectoration gave the murexid reaction, but did not show crystals. August, 1905: Had a sudden gush of offensive discharge from his throat, which caused nausea and vomiting. Examination of discharge showed pus, blood and leucocytes. September, 1905: Saw a consultant, who found an excavated ulcer in the left vocal cord. Mercurial treatment given for some weeks. September 26: Sputum gave murexid reaction, under the microscope no crystals, but masses of small lymphoid cells and round cells of carcinoma. Had now marked

<sup>1</sup> See *Brit. Med. Journ.*, 1911, ii, p. 1678.

<sup>2</sup> *Lancet*, 1893, ii, p. 1500.

stridulous breathing and dyspnœa. Much pain over and round the larynx. October 2: Taken to Golden Square Hospital, where tracheotomy was performed next day. Went home after three weeks. Rapid infiltration of the larynx followed, and he sank and died on January 22, 1906.

Dr. Gayford says: "At the time this case greatly impressed me. It seemed impossible to discount the conclusion it thrust home—viz., that surely there must be in some cases a close relationship existing between a gouty condition and incipient cancer."

Personally, I think there is so close a relationship that if this patient had been treated with solvents of uric acid in place of mercury and iodides, which act as retentives, driving it into the tissues and increasing the local injury it produces, the case might have had a different ending. It would be difficult or impossible to find a case better suited to illustrate the researches of Mr. Ross and Dr. Cropper.

To escape both stages of the process (gout and cancer) you have only to live as a poor man, avoiding uric acid and leading a frugal, laborious life; for the relation of gout and malignant disease to poverty is but an expression of the fact that many foods, rich in uric acid, are both relatively and absolutely expensive, and that diminished food and hard work favour the elimination of uric acid from the body. Thus the prevention of the one is also the prevention of the other, and I believe it will more and more appear that the treatment of the one is the treatment of the other, that what does good in gout does good also in malignant disease, and that what does harm in gout does harm in malignant disease.

It thus comes about that I am the advocate of a treatment by diet which costs but little, can be used in every case, does not prevent other treatment, indeed it favours operative treatment. It can also be used with some hope of success in preventing recurrence after operation. Dr. Horder suggested, in reference to my treatment, that a diet which causes debility should not be made use of in a wasting disease. There is here a double misunderstanding, for first of all cancer is, as we have seen, a disease of the strong and well nourished, and, secondly, the uric-acid-free diet need not cause any debility if carried out properly. Of some cases at present under my care it is not too much to say that they are doing well, and a case of carcinoma mammae at present under my son's care has gained half a stone in four months on a rice, curd and milk diet.

I believe the relationship of malignant disease to gout gives us the

key to causation, prevention and treatment, and chronic gout eventually gives rise to much wasting and debility, but it is none the less a disease of the rich and over-nourished, and only affects those of the poor who take much uric acid in meat, tea, meat extracts, &c. In my opinion, Dr. Horder has been looking in the west for the sunrise—he will not see it there. Let him look in the east among the poor and those that live frugal and laborious lives, and he will see that malignant disease is not a thing they need to fear, except through imitation of the depraved and luxurious west.

I am quite aware that a meat diet will under certain conditions cure gout or rheumatism. This was pointed out to me many years ago in a medical journal in New York, and they were good enough to publish my explanation of the facts. But such cure is at best a temporary one, as it deals with results and not with causes. In the same way many metals such as copper, mentioned in this debate, or the iodides, will under certain conditions cure gout, but here again we have a mere temporary cure, a treatment of symptoms, not a removal of causes. To keep a wound open and constantly discharging will sometimes cure or prevent gout, and it is interesting to see that a similar treatment has been suggested for malignant disease.

To say that a case of malignant disease has retrogressed spontaneously is merely to state an observed fact of which we have no explanation. There must be a cause for the retrogression, and that cause may well be the one suggested in this paper—viz., an increase of the power of the body fluids to hold uric acid in solution—which we can now see conditions many of the relationships of malignant disease to time of life, just as the solubility of uric acid explains the relation of malignant disease to special portions of the body.

The steady increase of malignant disease on a line parallel to gout and several other important diseases which are clearly due to uric acid is confirmatory evidence as to the causation of malignant disease, which cannot be much longer overlooked.

In conclusion, I will merely point out once more that diet treatment can be used in every case as soon as it is seen, and, when operation is necessary, a natural and correct diet places the patient in the most favourable position both to withstand the shock and to repair the wound.

Dr. ROBERT BELL: I have listened with great interest to all that has been said by the previous speakers upon this important subject, and regret that I have been unable to gather much encouragement from the

results that have followed the various lines of treatment which have passed under review. It is not surprising, therefore, that so far as the views expressed are borne out by facts, there seems to exist in the minds of those who have previously taken part in this discussion an amount of pessimism which from my point of view is hardly warranted, and my reason for making this remark is, that the speakers have, in my opinion, not taken a sufficiently wide grasp of the therapeutics of cancer. Moreover, I maintain that until we arrive at a correct notion of the natural history of the disease in *man*, which we shall never accomplish by studying tumours in mice and other small animals, and imagining that they have any relationship whatever to cancer in the human body, we shall be compelled to rest content with our present limited knowledge of the subject. It is not my intention, however, to refer further to the methods which have been tried and failed, than to state that so long as therapeutic measures are based upon the present generally accepted dogmas and theories, regarding the origin and nature of cancer, so long will it baffle all who attempt to treat it either therapeutically or surgically.

It is too elaborate a subject to go into in detail during the time at one's disposal in a discussion, such as this, but it will not be out of place if I call attention to the fact that notwithstanding the thousands, nay, tens of thousands, of operations that have been performed upon patients suffering from cancer in recent years, the death-rate from this disease has gone up, during the period I have been in practice, over 200 per cent., and yet I maintain it is an easily preventable disease, and, with equal certainty, that it is a curable disease without operation. I have tried both methods, and, as it happens, for nearly equal periods, I operated extensively during seventeen years, and it is eighteen years since I gave up what was a lucrative part of my practice, because I could not bear the idea of looking forward to the inevitable recurrence.

I was quite aware of the fact that Nature not infrequently accomplished a cure in cancer. Therefore, there should be no reason why careful investigation should not result in obtaining some knowledge of Nature's methods. One's first object, then, is to arrive at some idea as to the circumstances which invariably accompany the incidence of the malady, and which have long been prominent before the resisting power of the cells to disease had been overthrown, and a fitting soil for the development and growth of cancer been simultaneously provided. The next was to compare the mode of life which prevailed in countries most afflicted with cancer, and compare that with countries where it is practically non-existent. It then became apparent that diet exercised an



important influence upon cancer statistics, and if we examine these carefully we will find that the more a community departs from the strict observance of those physiological laws which point unmistakably to what our diet should consist of, the more will we find disease of every description to prevail, especially cancer, rheumatism and gout, all of which diseases take origin in the colon.

It was my privilege to be the first to call attention to intestinal stasis as the incentive to auto-toxæmia, and I believe, also, to point out the intimate relationship between auto-intoxication and cancer, and not only cancer, but also those diseases which have been described as being due to the presence of uric acid in the blood. This, I aver, is only a product dependent for its existence upon intestinal stasis, especially when that is associated with a highly nitrogenous diet, the fermentation of which in the colon produces toxins of the most virulent description, and also invariably tends to promote constipation. Now it is impossible to have toxæmia persisting for any length of time without the metabolism of every cell of the body becoming prejudicially affected, and consequently the thyroid and other important glands are rendered incapable of exerting their salutary influence upon the blood-stream. The direct consequence is that physiological control over cell life ceases, this being replaced by a condition of things which is not only antagonistic to healthy metabolism, but has succeeded in extinguishing that vitalizing influence which hitherto had been so characteristic of healthy cell life. Is it to be wondered, then, seeing a suitable soil for an unhealthy development and growth of perverted cell life has been provided and maintained, that morbid conditions supplant those of the normal?

I think it will be conceded that the most instructive and masterly essay upon intestinal stasis and its surgical treatment by Mr. Arbuthnot Lane, which has recently been published, confirms in every particular that which for years I have been endeavouring to convince my professional brethren is one of the most, if not *the* most, important of factors in the production of cancer. There is one never absent circumstance which has been present in every one of the numerous cases of cancer that have come under my observation, and that is, the onset of the disease has been without exception preceded by obstinate constipation. Indeed, I have no hesitation in affirming that even notwithstanding all our present dietetic errors, if the individual cultivates a complete evacuation of the colon every twenty-four hours, his or her chances of escaping cancer are enormously increased, whereas if this condition is coincident with a reformed diet he or she need have no fear whatever of this and many other diseases.



The first and most important line of treatment consists in directing special attention to the sanitary condition of the colon, a reformed diet and the administration of the active principle of the thyroid gland, sometimes alone or with the addition of thymus gland. By those means alone I have obtained most satisfactory results, a number of recoveries of patients dating back to 1895, many of those being still alive and well. Of course, there exist a number of adjuncts to treatment which I have had recourse to, and on a fairly extensive scale, such as the inter-muscular injections of atoxyl, colloid of copper, colloid of selenium, &c., the local application of X-rays, radium, and the frequent douches of air raised to a temperature of 300° F., and applied frequently at a pressure of at least three, but in many instances of four, and even five atmospheres. The heating up of the neoplasm would seem to exercise a highly satisfactory effect upon the pathogenic structure, while the therapeutic, dietetic, and sanitary measures exercise a beneficial influence upon the blood-stream, thus promoting the return of healthy cell activity. By so doing we deprive the neoplasm of its source of nourishment, which, as a matter of course, must lead to its destruction.

My contention is that if cancer is, in the early stage, treated by the method I advocate, that it is as curable a disease as any other, and that even in more advanced cases it is more amenable to therapeutic than to surgical measures. Of course, one meets with disappointments at times, but these will occur with decreasing frequency as our knowledge increases. What is wanted is an open mind and a more accurate conception of the conditions of life, which being so openly out of harmony with physiological and dietetic laws not only open the portals to disease but actually invite its entrance.

In conclusion, permit me to state that I am not opposed *in toto* to the removal of cancerous neoplasms by the knife or by any other means, but what I do take strong exception to is the plan so universally practised of leaving the patient in exactly the same vulnerable condition which permitted the disease to assert itself in the first instance, thus giving every facility to its reasserting itself in the tissue so terribly weakened by the operation. It stands to reason that were therapeutic, dietetic, and sanitary measures adopted prior to and after an operation, the prospects of recurrence would be reduced to a minimum. This plan should surely appeal to the common sense of every man who is possessed of an open mind, as it is impossible that anything but good could result were it generally adopted.

Dr. OTTO GRÜNBAUM said that he was a pessimist. He had no cure to offer, but he wished to place on record some of his experiences. Several of these occurred several years ago. In 1905 he was asked to see and suggest treatment of an advanced case of cancer. The friends of the patient had been told by an eminent surgeon that six weeks was the longest that they might expect life to be prolonged. The ovaries and uterus had been removed some years previously, and malignant disease had recurred in the lymphatic glands. There was considerable œdema of the right leg, which he thought might be due to the contraction of fibrous tissue around the vein, and at that time fibrolysin was a comparatively new drug, and he suggested that it should be tried. In February injections of that drug were begun; the œdema gradually diminished, and in May the patient left her bed. In August the patient went to Boulogne and was much annoyed that she did not obtain permission to bathe. If he had published the case in August, 1905, instead of February, 1913, he might have been led to advocate fibrolysin in the treatment of cancer. The patient died in the following July, eighteen months after a verdict of six weeks of life had been passed. He quoted the case in order to illustrate the danger of drawing hasty conclusions. He was of opinion that if any new treatment which was not based upon experiments on animals appeared to do good, the observer should not rush into print, but continue his work for two years, and not publish improvements which occurred during the first weeks of a new treatment. A well-known physician had once advised a colleague to use a new drug whilst it still cured. He thought that this might apply to the various colloidal metallic preparations which are at present said to cure cancer. About 1903 his brother had injected a cow with disintegrated breast cancers; his brother had used the serum of the cow, and related his experience in his recent paper. He thought that the milk of the cow might contain a cytolytic substance, and that by administering the milk to patients a large quantity of this substance might be introduced without leading to serum disease. His hopes were not gratified; marked improvement did not follow the administration of the "cytolytic milk." He had tried many so-called remedies. He had injected pleural effusions; he had drawn blood from patients and injected the autogenous serum. He had injected pig's blood and tried a large number of methods which had been said to do good, but, unfortunately, his experience of them all had been that they did not prevent the growth increasing and the patient dying. Though a pessimist, a recent observation made him believe that some day a cure would be found. A short time ago he had in hospital a

patient who had developed tumours upon the femur, pelvis, upper jaw, and lower jaw. Mr. Milne diagnosed these as a form of osteomalacia. The administration of suprarenal extract led to complete recovery. The introduction of dried gland by the mouth, leading to a profound alteration in the metabolism of certain cells, seemed to him to be a hopeful sign.

DR. J. A. SHAW-MACKENZIE: In the course of the paper read by the opener of this discussion reference was made to the so-called "trypsin treatment." As this treatment was commenced by myself entirely independently of any other theory or investigator, I am glad to have the opportunity of explaining one or two matters in relation to it.

My first point is a personal one, for I do not think it is fully understood by the profession that I have had nothing to do with the "trypsin treatment" advocated in the lay Press; moreover that treatment is not in any sense the trypsin treatment which I introduced. My method consisted of subcutaneous injections of trypsin together with the administration of pancreatic extract, duodenal extract and bile preparations by the mouth. The latter part of the treatment seems for the most part to have been overlooked. On the other hand, the notoriety gained in the lay Press refers to the employment of injections of trypsin supplemented by injections of amylopsin. I stated my objection to this method of administration of trypsin some years ago, and these objections I still more strongly hold. Is not such a method a misconception? For it is generally known that the introduction of an enzyme is followed by the production of its antibody. If, therefore, enzyme action is intended, it follows that the employment of trypsin, or any other enzyme, defeats its own object, namely, reaching the site of the disease at a distance. It is also well known that the pancreatic secretion has in itself no tryptic power, the trypsinogen in the juice having to be activated first; this is normally accomplished by the enterokinase of the intestinal juice; it was this, partly, that led me to recommend the use of duodenal extract in addition.

As our knowledge of metabolic action in the body cells has increased it has been abundantly shown that the majority of the chemical transformations which occur intracellularly are carried out by enzymes. These intracellular enzymes may not be identical with those which occur in the alimentary tract, but at any rate the effects on proteins, carbohydrates and fats are substantially the same in both cases. One can hardly doubt that in disease part of the symptoms are due to

irregular or abnormal activities of the intracellular enzymes, due either to their absence, deficiency, or excess, or it may be to the presence of unusual enzymes.

Attention has also of late years been directed to substances known as co-enzymes, the activators or accelerators of enzyme action. One of these, enterokinase, I have mentioned already; I might also refer to the internal secretion of the pancreas, which is believed by some to contain the activator of the glycolytic enzyme.

The rationale of enzyme treatment in carcinoma will be gathered from the preceding remarks. One is justified in concluding that in this disease there is an upset of the normal course of enzyme events, because the blood of these patients manifests a marked change in its reactions. The opportunity of prosecuting work on the blood and the modifications it exhibits as the result of the injection of various tissue extracts and other substances in animals (mice) has been afforded me by Professor W. D. Halliburton, in the Physiological Laboratory at King's College, London. Whilst working there, Dr. Otto Rosenheim suggested that lipase, the fat-splitting enzyme of the pancreas, should be taken into account, and since then in various communications I have published, partly in conjunction with him, preliminary accounts of the results obtained. Rosenheim showed that the lipase contained in glycerine extracts of the pancreas can, by filtration, be separated into two inactive portions. On mixing together the residue on the filter and the filtrate the mixture exerts the same fat-splitting action as the unfiltered extract. The residue on the filter (*inactive lipase*) is destroyed by boiling, but the other component, namely that in the filtrate, is thermostable; this second substance is termed the *co-enzyme* of pancreatic lipase.

Therapeutic preparations of the pancreas contain practically no lipase, but they do contain the co-enzyme. In the light of present knowledge it is just possible that the therapeutic effect of trypsin may be attributable to this co-enzyme. *In vitro*, preparations of trypsin, whether boiled or unboiled, increase the fat-splitting action of lipase, and *in vivo* injections lead to a great increase in the power of the serum to accelerate fat-splitting action. The action of pancreatic lipase is accelerated also by bile salts; and the same property is shared by many other hæmolytic substances. It is for this reason I attach further importance to the administration of preparations of bile or bile salts in my method. On the other hand, cholesterin was found to exert an inhibitory influence. It should be recollected also that the late J. H. Webb, of Melbourne, recommended the administration

of preparations of bile by the mouth, together with subcutaneous injections of sodium oleate, in the treatment of inoperable cancer, on the assumption that cholesterin in the tissues was a determining factor in the causation of cancer.

Various tissue extracts and serum of animals were found also to have a similar activating and accelerating action on lipase. In serum and serous fluids obtained from cases of malignant disease and in certain other pathological states, the activating and accelerating action is markedly increased; whilst cholesterin here also was found to exert an inhibitory influence. The activating and accelerating action is well marked in serum and serous fluids (œdema, ascitic and pleuritic) in malignant disease. I found the same in mice inoculated with malignant mouse tumour; as also in mice which proved "negative" to inoculation, and in mice which had recovered spontaneously from large growths.

It seemed to me, therefore, that this property was not a mere accident, but that increased fat-splitting may be one factor in the natural defensive or protective processes of the body. Furthermore, I found in some four cases which I have had an opportunity of examining, that the activating and accelerating action of the serum was present four to five years after recovery from malignant disease. On the other hand, the antitryptic action, which is usually increased in malignant disease, was normal or subnormal. Two of these cases, noted by me in a paper I read before this Section in March, 1912,<sup>1</sup> are instances of the beneficial influence I think I obtained with pancreatic and intestinal extracts and bile salts by the mouth, in certain cases of inoperable or recurrent cancer; or as an adjunct to operation. They form but a small portion in comparison with cases in which such treatment exerted no immediate or ultimate effect on the growth, though improvement in general health and increase in weight have been noticeable in various cases over considerable periods of time. Another of the cases in which the blood was examined was that of abdominal sarcoma, which recovered under treatment by Coley's fluid, reported by Major Spencer, referred to by Mr. Rowntree. On this subject, I may say that I have witnessed in one case superficial sarcoma, recurrent after two operations, recover under pancreatic and intestinal extracts in conjunction with bile salts by the mouth, with no recurrence four years later. On the other hand, I have seen a case of sarcoma run its course in six weeks from beginning to end, unchecked

<sup>1</sup> *Proceedings*, 1912, v, pp. 152-164.

by Coley's fluid. Nor is it likely in such fulminating cases that anything could avail.

In the same paper I mentioned that in view of the remarkable activating and accelerating action of the serum on lipase, in malignant disease and after recovery, I had been led recently to commence further treatment by injections of the patient's own serum; bile salts being given also by the mouth. I noted two cases—one inoperable uterine and one inoperable breast cancer—which appeared to be doing well under such treatment. In both of these cases the fat-splitting accelerating action of the serum remained high under treatment, and the antitryptic power returned to normal or subnormal. It is now some months since treatment was suspended, and I understand that both patients are in good health at the present time. I must add that in a recent case of recurrent uterine cancer after operation, similar treatment had no effect in staying the growth, though the general health appeared to have benefited and an increase in weight was noted.

The treatment by serous fluid or by serum was first commenced by Dr. C. Mackay, of Lochcarron, on clinical observation. In 1907 he had under his care a case of carcinoma of the breast, with double pleuritic effusion. The fluid became absorbed, and coincident with this the carcinomatous masses became absorbed also. He inferred, therefore, that the fluid contained protective substances, and he suggested treatment by serum and serous fluid injections subcutaneously. A similar association and retrocession of growth was reported by Beebe, of New York. This case was primary breast carcinoma with hepatic metastasis and ascites. Various cases were treated with the fluid, apparently with some success. I was interested to hear that Dr. Horder had not been favourably impressed with the results in some cases treated in a similar way. At the same time it may be hoped that further trial may be made in this direction.

There are two further points I should like to mention; one of these is a detail in technique. Finding that I could not always get enough serum by hypodermic withdrawal of blood in the usual way, and that I was probably not giving enough, I have lately started blister exudate. The reactions of such fluid in carcinoma are similar to serum, namely, increased fat-splitting accelerating action on lipase and increased antitryptic power. The blister fluid in a healthy person is similar to normal serum. The other point is that such injections have been followed by diuresis—so far as I have gone—just as diuresis has been noted following therapeutic injections of serous fluid in non-malignant

conditions. In this connexion, it may not be without interest to mention that in one of the carcinomatous breast cases of recovery under treatment, notes of which Webb sent me, hepatic metastasis with ascites existed. The fluid was repeatedly withdrawn, but later it went. The note at the time was that "the abdomen emptied itself apparently by the kidneys, as the patient passed enormous quantities of water." A similar diuretic effect, Dr. Mackay tells me, occurred in the pleuritic effusion and breast carcinoma case, in which spontaneous cure took place. He tells me also that he too employed blister fluid in a subsequent case.

(The discussion was adjourned until March 18.)



## Therapeutical and Pharmacological Section.

March 18, 1913.

Professor W. E. DIXON, F.R.S., President of the Section, in  
the Chair.

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### Discussion on the Non-operative Treatment of Malignant Disease.<sup>1</sup>

#### SUMMARY AND REPLY.

By T. J. HORDER, M.D.

IF I may presume to say so, I think the Section is justified in having embarked upon this discussion. The venture has demonstrated the wide interest taken in the treatment of inoperable cancer, and has revealed the fact that a large number of Fellows of this Society are actively interested in this most pressing subject. Before the energy displayed in the mass of practical work in tentative cancer therapy undertaken by some of the speakers, as by Dr. Copeman for example, I stand amazed and humbled. There are, of course, culs-de-sac into which we are bound to wander, and will-o'-the-wisps we are bound to follow; this is inevitable; virtue lies in a quick recognition of the futility of proceeding further along any line which is clearly seen to be fruitless. In this way we shall best utilize our time and our resources.

The discussion has been singularly fortunate in eliciting representative opinion as to the present efforts in cancer treatment. In my short concluding remarks I will try to summarize these opinions. In doing so, I have no wish to act the critic, or, if that is a task I cannot well escape, I hope to act the impartial critic.

A full consideration of radio-therapy quite properly occupied much of our attention; as I pointed out, it is certain that to-day this method

<sup>1</sup> Adjourned from February 18.

has most successes to place to its credit, partial though these are in the great majority of instances. Dr. Lewis Jones is frankly pessimistic as to the present, and perhaps as to the immediate future, of this therapeutic measure; the weight of his authority and practised judgment must necessarily influence us greatly. Dr. Jones is of opinion that the good results of radio-active measures are probably produced by stimulation of the healthy tissues rather than by destruction of the cancer cell—in the case of carcinoma, at any rate. I incline to agree with him, and I hoped to hear more from Dr. Knox, Dr. Finzi, and Dr. Iredell concerning the effects of X-ray applications made to the body as a whole rather than to the malignant tissue. Perhaps the time is scarcely ripe for conclusions in this direction. Direct stimulation of the adjacent normal tissues and indirect stimulation of the body as a whole would be, perhaps, a poor exchange for the present hoped-for destruction of cancer cells by their immediate bombardment; but if observations point to giving this exchange a good trial they should be followed and the method should be pushed to its uttermost point of efficiency. Dr. Knox's experience of the great value of raising the general resistance and of improving the haemoglobin content of the blood seems to confirm Dr. Jones's views, though I gather that Dr. Knox still holds out hope of actual cancer cell necrosis as a direct result of radio-active measures. Dr. Finzi certainly holds out this hope, and his enthusiasm is welcome accordingly. Dr. Iredell's lament that in the end it is the cancer cell that is at fault, and not the radiations, is but a new expression of a provoking fact—namely, that the interaction between the therapeutic agent and the morbid element ceases before the latter has been completely overcome. Dr. Iredell's conclusion seems rather to denote that he also is not optimistic as to ultimate cancer cell destruction by these measures. The problem evidently is, how to continue and how to enhance the first good effects. The solution must lie, as Dr. Jones suggests, in an elucidation of the exact mode of action of radio-active measures, so that we may make this mode of action more efficient and more specialized.

Professor Grünbaum, as would be expected of him, rests his contribution to treatment upon a purely experimental basis. I refer to the use of anti-venom serum. The measure deserves thorough trial; even if it is not itself successful, the underlying experimental fact may well lead to the establishment of other valuable data. Dr. Shaw Mackenzie's efforts have been scarcely less methodically controlled, but they have suffered, as I hoped I made clear in my opening remarks, from a too

ardent exploitation by others. I am afraid it is obvious, from the present apathy in regard to the method—an apathy I cannot but feel is justified by the negative character of the results—that the remedial value of trypsin must be re-established before it finds fresh advocates.

Dr. Herschell's account of his experiences with colloid copper are very suggestive and are confirmatory of foreign workers. But are we not asked to believe too much? I refer to Dr. Herschell's statement that French physicians claim 26.7 per cent. of cures by the method. Personally, I should feel happier about Dr. Herschell's own results had the criterion which I laid down in the matter of diagnosis been observed in his cases. In the absence of this criterion, that is, in default of proof that the lesions were actually cancerous, the most we can say is that the cases quoted are highly suggestive. Statements amounting at most to presumptive evidence cannot possibly suffice for proof, and we might even question some of these statements, such as that "simple gastric ulcers do not occur in men aged 40," or that 42 per cent. of 6,000 leucocytes being lymphocytes is "strongly suggestive of malignant disease." Dr. Grünbaum made a striking reference to the improvement, often considerable, which, in particular cases, not infrequently follows a certain line of treatment that has no specific value in cancer as a whole, and preached forbearance in publishing any case in which a cure, or relief, had not lasted for a period of two years. I heartily endorse Dr. Grünbaum's suggestion. Dr. Herschell's cases are all very recent, and in one of them the treatment had only begun twenty-one days before our discussion opened. No doubt Dr. Herschell would say the case was quoted because some improvement had already occurred. But mere improvement, as already remarked, even in cases proved to be cancerous, which this case was not, will oftentimes follow any one of a large number of different remedies.

Mr. Rowntree's remarks were concerned with a variety of useful and very practical palliative means of dealing with incurable patients, and his contribution to this side of the subject will doubtless be welcomed by many whose practice includes these difficult cases.

It is, of course, no function of mine to chide a speaker for introducing statements that appear to my individual intelligence rather loose and unproven. But in being asked to sum up the discussion I have a right to point out the difficulty these statements put me into. Thus, Dr. Bell says that "gout, rheumatism and cancer all arise in the colon," but as he gives us no evidence for the correctness of his assertion all his remarks about treating cancer by correcting intestinal stasis must fail to

arouse interest. It is quite true that if the present experiments in removal of, or short-circuiting, the colon become the vogue we shall be able to test this notion of Dr. Bell's in the future, because if there is anything in it none of the patients in whom this operation has been performed will develop cancer. But at present we can only consider the assertion referred to as a pious expression of opinion. When Dr. Bell says "obstinate constipation always precedes cancer" we are faced not with a statement which we cannot controvert and which he cannot prove, but with an assertion which almost universal experience will surely deny. "Cancer is a preventible and curable disease," says Dr. Bell, and his subsequent remarks make it quite clear that he is referring to present, not to future, therapeutic measures. Yet this optimism is sadly impeached by the variety and by the heterogeneous nature of the remedies which he suggests: a vegetarian dietary, thyroid and thymus extracts, atoxyl, colloid copper and selenium, X-rays, radium, "hot air under pressure," and removal of the colon. What faith can he expect us to have in the curability of a disease which indicates the use of such a hotch-pot of treatment? So little faith that when he vouchsafes the remark that this programme "disappoints at times," he can scarcely expect us to evince surprise at hearing the confession.

Dr. Haig follows Dr. Bell very closely in many of his notions concerning the treatment of cancer. He is less optimistic as to present results, but only, I gather, because of lack of opportunity for a full trial of his dietetic measures. Dr. Haig's thesis is, we are not surprised to learn, the very familiar one of the dependence of the cancer process upon the retention of uric acid in the body. I think we all came to this discussion with open minds, but Dr. Haig's argument has seemed to me, at all events, provokingly unconvincing and inadequate: the precursors of uric acid cause cell proliferation; cancer is a form of cell proliferation; therefore, cancer and gout are similar processes, or are sufficiently allied to call for the same treatment. Dr. Haig tells us that gout and cancer affect the same situations, and whilst we turn our thoughts to the breast, the uterus, the tongue, the stomach, wondering what gouty affections of these organs in particular we have seen, he still further surprises us by an incidental reminder of the difficulty in the differential diagnosis between gouty and "malignant arthritis." Sarcoma of the heads of bones I know, and rarely of a synovial membrane, but what may "malignant arthritis" be?

Let me now conclude. The note of pessimism as to the present

state of our armamentarium has been struck by several speakers, and I find it impossible to pitch my own final remarks in a different key. But provided we are discontented with the present only, I do not think we need fear to face the obvious fact that we are not curing inoperable cancer. In the true sense of the word even the operable cases are not *cured*, for to excise an organ affected by a disease can scarcely be spoken of as curing the disease. We must continue with our present methods, adding fresh ones as they are revealed by observation and by experiment, until the problem shapes itself more clearly and the solution arrives.

### **The Action of Drugs on the Respiration.**

By A. R. CUSHNY, M.D., F.R.S.

THE pharmacology of the respiratory centre is of considerable interest from the therapeutical point of view, because occasionally one wishes to increase respiration by some stimulant method; and, while one never, I think, purposely attempts to reduce respiration, one is met by the fact that in certain treatments, notably in the treatment of various forms of cough, the respiratory centre is depressed. A great deal has been done of late years to elucidate the physiological mechanism of respiration and the action of the respiratory centre, and much of the vague knowledge has been crystallized by the work of Haldane particularly, and by that of Pembrey and others, who have worked for a long time and with very great success with regard to this centre. And it has come out quite clearly, what was somewhat hypothetical before, that the respiratory centre depends for its activity very largely upon the gases which circulate in the blood. The other factor in the activity is the nervous control, the control of the centre by reflexes whose afferent path is mainly in the vagus nerve, although other nerves are also involved. Another feature is that the main function of the centre is to change a constant stimulus due to the tension of the carbonic acid in the blood into an intermittent activity, parallel to the way in which a circular movement may be changed into a to-and-fro intermittent movement by various mechanical devices.

The action of drugs upon the centre is somewhat more complicated in the respiratory centre than in most other parts of the central nervous system, because the amount of carbonic acid in the blood is so often

altered under them. For example, if a drug slows the respiration, that in itself tends to accumulate carbonic acid in the blood, and this accumulation increases the activity of the centre, so that one might expect, theoretically, that any depressant of the respiratory centre would provide its own antidote by providing more carbonic acid. On the other hand, if a drug accelerates or deepens the respiration, this must tend to remove the carbonic acid from the blood, and hence to lower the activity of the centre, so that a stimulant ought, if things were properly arranged in the centre, to provide its own antidote. As a matter of fact, we find that is not part of Nature's plan at all. Another point that must be remembered—one which caused me much grief at first—was the difficulty that any movement, apart from the regular respiratory movement, causes carbonic acid formation. So that an ordinary depressant drug has a complicated action: it lessens twitching of limbs or any other movement, and thus reduces the carbonic acid tension and so tends to lessen the activity of the centre indirectly.

My experiments were carried out first upon myself, but finally, as I could not analyse them properly, I had to resort to decerebrated rabbits, so as to get an analysis of the way the drugs act on the centre. The first drug I took up was morphine, since morphine is used more frequently and affects the respiration more directly than almost any other; and there is some question as to how far it depresses it and how far its action on the respiratory centre is a necessary concomitant of its action in other parts of the body. It has long been known that morphine slows the respiration, and everyone has been able to confirm that abundantly. But another point is, that under morphine the centre becomes less sensitive to carbonic acid, as Loewy showed many years ago. My routine procedure was first to investigate the sensitiveness of the centre of respiration by giving a certain strength—5 per cent.—of carbonic acid, then to inject morphine and to examine it again; the 5 per cent. carbonic acid has now considerably less effect in accelerating respiration. One can inhale considerably stronger mixtures of carbonic acid when morphine has been taken than when no morphine has been used. For instance, I found that in the normal condition I could only tolerate something like 7 per cent.  $\text{CO}_2$ , for with higher strengths the experiment became too arduous, and I was exhausted within a minute. Under morphine, however, I ran up to 10 per cent. or, to be exact, 10.5 per cent.—that is, my endurance of  $\text{CO}_2$  was 50 per cent. better. On the other hand, I found that morphine has very little effect on the depth of the respiration. A moderate dose



of morphine given to a rabbit may reduce the frequency perhaps 30 per cent., but the depth of respiration may remain unchanged. If carbonic acid 5 per cent. is inhaled after morphine, while there is less acceleration than in the normal animal the depth induced by the carbonic acid is the same as usual. This is shown in fig. 1, in which the rate and depth of the respiration in air and under 5 per cent.  $\text{CO}_2$  is shown throughout an experiment.

This decerebrated rabbit breathed 35 times in the minute. The depth was 28 to 30 mm. One-fiftieth of a grain of morphine was given, and the rate began to decrease from 35 to 28. Another dose caused a further fall, and so it reaches 18 or 19 instead of 35. The depth of respiration is scarcely changed, there being a rise of 1 or 2 mm. At intervals I took the respiration under carbonic acid  $4\frac{1}{2}$  per cent. In

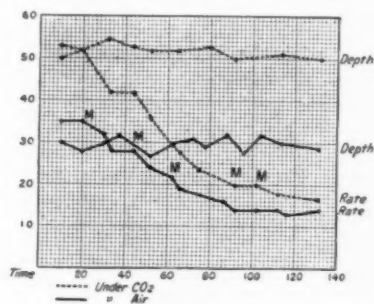


FIG. 1.

the beginning, before morphine, the rate promptly rose to 53 per minute, and the depth rose from 30 to 50 mm. Under morphine the carbonic acid lost its effect very considerably; for example, the rate under morphine was increased only from 14 or 15 to 17 or 18 per minute, while in the beginning the rate rose from 35 to 53. But the depth under carbonic acid remained unchanged. Fig. 2 is a chart in which an inhalation of carbonic acid was taken before and another after morphine. The normal respiration was 38. Carbonic acid was inhaled and the rate rose slowly from 38 to 50, the carbonic acid being somewhat dilute. It fell rapidly after the carbonic acid was cut off. The depth increases somewhat in the same way. Afterwards morphine was injected, and about fifteen minutes afterwards this same strength of carbonic acid was inhaled. The rate had now fallen from 38 to 21. The carbonic acid again accelerated, but to a less degree than before. The depth, however,



under carbonic acid in morphine poisoning remained very much the same as before the morphine was given. So this again illustrates the fact that morphine acts upon the rate, and not directly on the depth.

But when the dose of morphine is very large the effect is a little different, because large amounts of carbonic acid accumulate in the blood, and this causes stimulation of the centre. The centre is depressed, as far as rate is concerned, so that it cannot relieve itself of the carbonic acid by accelerating, as the normal centre would do. The effect of stimulation with carbonic acid is now only to increase the depth, and so there is a slow and deep respiration. For example, in a rabbit which was particularly susceptible to morphine, the respiration fell from 37 to 22 on 2 mg. of morphine, and the depth rose a little, from  $16\frac{1}{2}$  to 18 mm. Another dose of morphine reduced the rate from 37 to 8, or about one-fifth the normal. This was sufficient to cause carbonic acid excess, and the depth rose to 22, in order to eliminate the excess of  $\text{CO}_2$  in the blood. Under carbonic acid inhalation the respiration was no longer able to respond as at first with 50, and finally it rose only from 8 to 9; it can only respond with one respiration more per minute, and hence the depth increases to a remarkable extent, to 28, instead of 22 or 23. And this is the reason why, in certain cases of morphine action, there is very slow and very deep respiration. Caffeine, 20 mg., injected at this point, caused the rate to rise to 24, while the depth fell from 22 to 19, and subsequently lower, and the centre was now able to respond by a considerable increase to carbonic acid inhalation, from 24 to 31. There is therefore no necessity for the centre of respiration to deepen so much as it did before under morphine. When the centre is so deeply narcotized by morphine that it cannot accelerate under carbonic acid, the breathing often becomes very deep, and that is the only way in which it can respond to this excessive stimulus. I am emphasizing this a little because some misunderstanding has arisen on the matter in comparatively recent times; and I think that twenty years ago it was better understood than it has been in the last ten.

Codeine has very much the same effect on respiration as has morphine. There is the same fall in rate, the same loss of the power of acceleration, while the power of deepening still remains.

Another drug which has become prominent in the last few years is heroine, which has been supposed to act in a somewhat different way from morphine, and to have certain qualities which render it preferable to morphine in the treatment of cough. These supposed advantages appear to have arisen from the enthusiasm of the advocates of heroine

rather than from the intrinsic virtues of the drug. The statement is made that morphine slows the respiration and shallows it, while heroine, while also slowing it, deepens it, all of which is perfectly true. Morphine not infrequently shallows respiration if it reduces movement; it renders it more shallow because it lessens carbonic acid formation. But the degree of shallowness is trifling. The shallowing of the respiration under morphine means that the respiration is in a satisfactory condition. The deepening shows that there is an excess of carbonic acid in the blood, that the respiration is entirely insufficient, and that a condition of dangerous poisoning has been reached. The deepening in heroine is of exactly the same order. This deepening, which has been insisted upon by Dreser and Impens particularly, merely indicates that the respiration has been slowed so much by heroine that carbonic acid

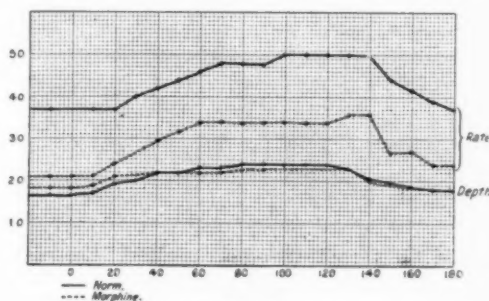


FIG. 2.

accumulates in mass in the blood. And if one looks over the figures of these observers on morphine and heroine action, one sees that the morphine slows the respiration very little in their experiments, and it may therefore be a little more shallow. That simply means that the respiratory centre is still fit to carry on its necessary function of getting rid of carbonic acid. On the other hand, the figures with regard to heroine show a marked fall in rate, so that the centre is obviously not in a condition to carry on the usual gas exchange, and thus the respiration becomes deeper. The argument, therefore, is reversed. The fact that heroine deepens respiration by making it slower, indicates that heroine induces a condition of danger, while the morphine has not done so in the doses used. The fact is that heroine has a much more powerful paralyzing effect on the respiratory centre than has morphine. Heroine depresses the centre in smaller doses than does morphine.

I thought it necessary to look into this matter of heroine because of the misconception which exists in regard to it. It is frequently said that heroine does not depress the centre in the same way as morphine does; but this is a mistake, for it depresses it in the same way and to a much greater extent.

Another point of difficulty in regard to morphine has been the explanation of its use in cough. It has been often suggested that morphine may lessen cough by hindering the arrival of afferent impulses in the motor part of the centre, perhaps by depressing the synapse of the vagus intervening between the vagus sensory fibres and the motor cells of the centre. But morphine acts exactly in the same way on the respiration of an animal in which the vagus has been severed an hour or more previously, so that this explanation of the action of morphine on cough does not seem sufficient. And on stimulating the vagus electrically one finds that in most experiments the response of the respiration to stimulation of afferent fibres is the same as before. So it seems difficult to suppose that the action of morphine in lessening the respiration is due to its cutting off sensory impulses. The clinical fact of its reducing cough is rather difficult to explain. One can only suppose that the slowed respiration is at any rate an accompaniment of the lessened cough. But how morphine reduces cough I do not propose to take up. As a matter of fact, the animals I worked upon are incapable of coughing under any circumstances. The rabbit does not cough at all; the cat coughs, but in a very irregular way.

My experiments show that morphine affects the  $\text{CO}_2$  factor rather than the nervous control of respiration, but its effects cannot be defined as merely reducing susceptibility to carbonic acid. For it only reduces the susceptibility so far as one feature of the response is concerned—namely, the rate. So one is compelled to take the view that morphine slows respiration neither by acting on the nervous regulators nor upon the carbonic acid regulator, but rather on the function of the centre which changes the constant series of stimuli into a rhythmic response.

The other two depressants which I have examined are chloral and urethane. Both of those reduce the rate of respiration while leaving its depth comparatively little changed, except in so far as they both reduce movement; and so they do not tend to cause the same deepening as in the case of morphine. Still, with large doses there is a very slow and deep respiration. The effect of these drugs on respiration differs from that of morphine in that it is so difficult to elicit it. The slowing is an early symptom with morphine, but chloral and urethane

in quantities sufficient to cause deep sleep have but little effect in slowing respiration. The following experiment on a decerebrated rabbit under urethane will serve to illustrate this point.

A DECEREBRATED RABBIT WAS ATTACHED TO THE APPARATUS FOR RECORDING FREQUENCY AND DEPTH OF RESPIRATION. URETHANE WAS INJECTED INTRAVENOUSLY.

| Time, minutes | Urethane in grammes | Rate per minute | Depth in millimetres     | Rate under CO <sub>2</sub> | Depth under CO <sub>2</sub> |
|---------------|---------------------|-----------------|--------------------------|----------------------------|-----------------------------|
| 1             | —                   | 44              | 21                       | 68                         | 30                          |
| 14            | 0.25                | —               | —                        | —                          | —                           |
| 16            | —                   | 40              | 17.5                     | —                          | —                           |
| 19            | 0.25                | —               | —                        | —                          | —                           |
| 21            | —                   | 32              | 20                       | 46                         | 32                          |
| 31            | 0.5                 | —               | —                        | —                          | —                           |
| 35            | —                   | 30              | 20                       | —                          | —                           |
| 37            | 0.5                 | —               | (Artificial respiration) |                            |                             |
| 49            | —                   | 28              | 22                       | 30                         | 30                          |
| 62            | 0.25                | —               | (Artificial respiration) |                            |                             |
| 68            | —                   | 26              | 22                       | 23                         | 26                          |
| 78            | —                   | 23              | 27                       | 20                         | 30                          |

The effect of the first dose was to lessen muscular movement and thus to reduce the CO<sub>2</sub> of the blood and the depth of respiration, while the effect on the rate was very slight. There is comparatively little change before the thirty-fifth minute, though the animal had received 1.0 gr. and was very deeply narcotized. The rate had fallen to 32, but the depth was practically normal. Another  $\frac{1}{2}$  gr. stopped the respiration promptly, but it was restored by artificial respiration. Under CO<sub>2</sub> it rose to 30 in rate and 30 in depth, so that the centre was only temporarily put out of play. It is interesting to note that the carbonic acid, instead of accelerating the respiration, sometimes slows it. I am not prepared with an explanation of this point, unless carbonic acid itself is a respiratory narcotic, when the centre is deeply depressed. I have noticed this paradox several times with chloral and urethane, and perhaps some explanation may be suggested. The amount of carbonic acid seems small to act as a narcotic—namely, 4.5. This experiment illustrates another point which I have dealt with at greater length in the full paper to appear in the *Journal of Pharmacology*, that when the artificial respiration was in progress, the spontaneous respiration having failed, the centre began to respond to the inflation. As the air escaped the animal quickly responded with a spontaneous inspiration. I promptly stopped the artificial respiration, and there was no spontaneous respiration. The centre, therefore, responded to the reflex arising from the dilatation of the lungs, before it was capable of spontaneous respiration.

The failure of the respiration, therefore, could not have been due to failure of the afferent nervous impulses, for it responded to these after the respiration had ceased.

I tried two stimulants to respiration—namely, caffeine and strychnine. Caffeine, as a rule, accelerates, and at the same time often renders the respiration rather shallow. In other cases in which the large dose of caffeine causes spasmodic movements both rate and depth are increased. The increase in rate is due to direct action on the centre, for it occurs when no movement is present and when the depth of the breathing is actually reduced. The deeper breathing observed in some experiments occurred only when movement was present, and passed off as the animal became quiet again, so that it appears to be due to the increased  $\text{CO}_2$  tension from the movement. As the caffeine action passes off, which it does very rapidly, one finds a return to the normal. Caffeine acts in the opposite way to morphine, and the same is true of strychnine. They act upon the rate, but not directly on the depth. The changes in the depth are due almost entirely to change in the carbonic acid tension, which, of course, is largely indirect, from the acceleration of the respiration reducing it, or from slight spasm increasing it. The action of caffeine is very much more marked under morphine, and its action persists for a much longer time. In normal animals there is an acceleration under caffeine, which, as a general rule, passes off in ten minutes at the most. Under morphine it may last half an hour or so after the injection. Under caffeine I saw, twice, on stimulation of the vagus, that a strength of stimulation that previously caused inhibition now caused acceleration; that is, a reversal phenomenon was presented by the respiratory centre, similar to that which has been described by Sherrington, Bayliss, and others, in the reflex response under strychnine. On the other hand, I did not get this reversal under strychnine because of the difficulty that strychnine, given in any but the most minute quantities, causes spasm, and spasm throws a burden of carbonic acid on the centre which altogether vitiates the experiment. But such a reversal under strychnine has been described by Seemann lately, who prevented the spasm by giving large doses of urethane. The animals with cut vagi respond by acceleration to caffeine and strychnine as intact animals do. The point arose whether caffeine or strychnine could replace carbonic acid in the action on the centre; but I have no evidence that this is so. On the contrary, they accelerate respiration after cutting the vagi, while carbonic acid fails to do so, which shows the different method of action.

## Therapeutical and Pharmacological Section.

April 15, 1913.

Professor W. E. DIXON, F.R.S., President of the Section, in the Chair.

### Discussion on the Use of Salvarsan and Neo-salvarsan in Diseases other than Syphilis.

Opened by BYROM BRAMWELL, M.D.

DR. BYROM BRAMWELL, in opening the debate, said that when he was invited to undertake that function he stated that his experience of the drugs, except in pernicious anæmia, was so limited that it would not be worth anything at present, but he would be delighted to give his experience with salvarsan in cases of pernicious anæmia.

He would give a brief résumé of the cases of pernicious anæmia in which he had employed the drug, and leave his hearers to draw their own conclusions as to the results. It was now thirty-eight years since he treated his first case with arsenic, and he was now in a position to make comparisons of the effects of the two drugs. When salvarsan was introduced, it occurred to him that although arsenic did much good in a large number of cases of the disease, yet it only temporarily cured them, and therefore it might be well to try salvarsan.

*Case I.*—The first case in which he used salvarsan was that of a man, aged 49, an electric hoist man, formerly a soldier. He was admitted to Edinburgh Royal Infirmary on October 12, 1910. A year previously he had seen him, and treated him with arsenic, and he had temporarily recovered. In September, 1910, he caught cold, his anæmia relapsed, and he came into the Infirmary with all the symptoms in marked degree. The red cells numbered 1,035,000, and the colour index was 1.5. At first he was treated with gradually increasing doses of liquor arsenicalis until he was having 12 minims thrice daily. On December 21 he had 0.2 gm. of salvarsan intramuscularly, and three subsequent doses—namely, on January 5 and 19 and February 9. The chart (shown) proved that there was great improvement, the index coming down to practically normal. The blood was last examined on



March 7 last, when the red cells numbered 4,210,000, the hæmoglobin 85 per cent., and the colour index 1. In July, 1911, he marched 25 miles with the Territorials, from Kilmarnock to Troon, without difficulty. When the count in March, 1912, was made, Dr. Bramwell sent for the man to come to his clinic; it was at the time of the railway strike, and he accordingly had to walk 10 miles in order to reach the nearest point to procure means of conveyance; he arrived at the Infirmary fresh and well, and apparently had remained in perfect health.

*Case II.*—A woman, aged 40, who was admitted in November, 1910, suffering from pernicious anæmia of four months' duration. She was treated with increasing doses of arsenic with some improvement. On December 24 she was first given salvarsan, and had four doses in all. The reds increased from 1,450,000 to 6,210,000 on March 7, last year; hæmoglobin 120 per cent. and the colour index 0·9. A few days ago the red cells were 5,260,000, hæmoglobin 100 per cent., and the colour index still 0·9. In all his experience of pernicious anæmia he had never seen a result like that, in which the red cells mounted over the normal, by any plan of treatment. During the past two years she had had one or two attacks of biliary colic, and might have to be operated upon; but in other respects she remained in good health.

*Case III.*—A woman, aged 54, whom he had for a long time under observation suffering from pernicious anæmia. He first saw her in 1905, and she died in September, 1911. She was more than once in the Infirmary. When she came first her blood count was very low, but under arsenic and iron she made a very remarkable recovery; it was one of the few cases of pernicious anæmia in which he had seen iron, in the form of the Blaud pill, do good. She relapsed, and was readmitted in a very serious condition indeed. As a last resource salvarsan was tried, and the patient improved in a remarkable way for a time. She had another relapse, from which she slightly rallied temporarily. She discharged herself, against advice, and died on September 5, 1911. During her last stay in hospital she had severe hypostatic congestion of the right lower lobe.

*Case IV.*—A married woman, aged 41, who was admitted to the Infirmary on March 28, 1911, her illness having commenced in December, 1910. She had extreme pernicious anæmia; the blood count was very low, but the colour index not very high. She was first given salvarsan on April 6, and had another dose on April 21. The blood count and colour index both increased. She was a very intelligent woman, but very poor, and as she had heavy family re-



sponsibilities was obliged to discharge herself. She had no treatment after that, yet a year later when sent for he found her looking extremely well, compared with her former appearance. The red cells then numbered 3,880,000, and the colour index 0·7. The improvement had continued, and this month the reds were 4,110,000, hæmoglobin 75 per cent., and the colour index 0·9; yet in the interval she had done all her housework, including washing. She had had no treatment except the two doses of salvarsan.

*Case V.*—A man, aged 50, a mason, who was admitted to the Infirmary in May, 1911. His illness had commenced six months previously. He had two doses of salvarsan, but there was absolutely no improvement, and he died on June 24.

*Case VI.*—A man, aged 31, farm servant, admitted May 17, 1911, suffering from marked pernicious anæmia. He had three doses, but got worse, and his friends removed him. The reds were 600,000, hæmoglobin 19 per cent., colour index 1·6. It was not expected the man would live more than two days. On being taken home he remained comatose for ten days, and then began to improve. Dr. Bramwell met his doctor some time later, who told him the man was quite well. He came in November by request to be examined, and then the reds were 3,100,000, hæmoglobin 66 per cent., colour index 1·1. He remained well until February, 1912, when he had acute croupous pneumonia, and died. He had not had a blood relapse. Dr. Bramwell did not claim that the improvement in this case was due to the salvarsan, but it was worth while keeping the case in mind; and it was perhaps not unreasonable to suppose that the effect of the drug persisted many weeks, perhaps some months, after its injection. In two fatal cases which he had examined post mortem, the salvarsan was more or less encapsuled in the deep tissues of the buttock; so that it was probable a gradual absorption might go on for months.

*Case VII.*—A man, aged 55, admitted October 24, 1911, with very marked pernicious anæmia. He improved very considerably after one injection of salvarsan, but developed broncho-pneumonia, and died on November 5. He could not say whether the broncho-pneumonia had any relation to the salvarsan.

*Case VIII.*—A man, aged 25, an engineer, who was admitted on October 3, 1912. This was a very severe case of pernicious anæmia to look at, although his blood count was not as low as in many cases Dr. Bramwell had seen. In this case the pernicious anæmia developed at the age of 20. He was temporarily cured with arsenic, but had a relapse

in 1909; was again cured, and relapsed in 1910; was again cured, and had a second relapse in 1910. His fourth relapse was in January, 1912, when he was again cured. He was not in the habit of taking care of himself—he went for long drives in a motor-car, when he often got wet through, and he frequently neglected his meals. He then came with his fifth relapse of pernicious anæmia, and had two injections of the drug; but there was no improvement, and he died ten days after admission. Dr. Bramwell's experience of salvarsan was much the same as his experience of arsenic—viz., that the first attacks did much better than relapses, and that after several relapses treatment was almost hopeless.

*Case IX.*—A man, aged 72, admitted on August 29, 1912, with very marked pernicious anæmia. His reds numbered 1,055,000, hæmoglobin 26 per cent., colour index 1·3. He had three injections of salvarsan and improved considerably. When discharged on December 6 he looked well and said he felt well. The reds were 3,450,000, hæmoglobin 75 per cent., colour index 1·1. Soon after discharge he relapsed, and was readmitted on March 3 in much the same condition as when first seen. He had one injection of salvarsan on March 11, and had remarkably improved; his colour was good, he felt better, and looked a different man. The fact that he relapsed so soon after his discharge was very significant, and he feared there would be other relapses, and that he would ultimately succumb to the disease.

*Case X.*—A man, aged 59, admitted to hospital on December 9, 1912; he had been ill a year. He had very marked pernicious anæmia, the blood being highly characteristic, with swelling of the feet, &c. After two injections he made a most remarkable recovery. It was one of the most successful cases he had ever seen. He last saw the patient on April 8 when he was walking about feeling well. His reds were 3,850,000, hæmoglobin 78 per cent., and colour index 1·01.

*Case XI.*—A man, aged 58, a railway guard, admitted January 11, 1913. He had been ill fifteen months, had been treated with arsenic, and had had more than one relapse. He did not look a bad case, and his red cells did not indicate that he was. He had three doses of salvarsan, and there was some, though not a great deal, of improvement; it seemed as if the remedy would not have much effect on him.

*Case XII.*—A man, aged 42, admitted December 16, 1912. He had been ill three years and nine months, and had been under the care of a distinguished London physician, who said the blood was in a very serious condition when he saw him. He attended at Edinburgh because of subacute combined paralysis—a typical case—associated with

anæmia. The colour index was 1·4; that was a point strongly in favour of pernicious anæmia. He had seen several cases, proved post mortem, in which subacute combined paralysis was associated with pernicious anæmia. He hoped that this man's anæmia would be improved by the salvarsan, but that hope was not supported, though there was some improvement in his general state. On February 22 the spastic stage was replaced by the flaccid, and he became much worse, and died on March 22. Post mortem, all the characteristic features of pernicious anæmia were found.

*Case XIII.*—A man, aged 41, admitted March 29, 1913. He had been ill, off and on, for two years, having had several relapses, which had been successfully combated with arsenic. He had one injection of salvarsan on March 30. When he came in the reds numbered 1,210,000, hæmoglobin 40 per cent., and the colour index 1·6. He was very yellow, the conjunctivæ were deeply stained, and his general condition was very unsatisfactory. So far there was no improvement following the one injection. When last counted, on April 4, the number of reds had fallen slightly—namely, to 1,150,000.

Dr. Bramwell had related all the cases in which he had given the remedy, whatever the result, and comparing the results with those he had achieved with arsenic, which he introduced in 1875, he was certainly favourably impressed with salvarsan. He had seen remarkable temporary cures under arsenic; but in any series of thirteen cases he had not seen such good results under arsenic as in these thirteen in which he had used salvarsan. The series showed that in some cases there was no apparent benefit, but in others there had been very remarkable improvement. Two years was the longest time since any of the cases were treated, therefore he did not know whether they were likely to relapse, but he regarded salvarsan as a remedy of very great use in the treatment of pernicious anæmia.

The PRESIDENT (Professor W. E. Dixon, F.R.S.) said it had been a great treat to him to listen to the fascinating and easily followed account which Dr. Byrom Bramwell had given of the effects of salvarsan and arsenic in the treatment of pernicious anæmia. He was himself unable to enter into a discussion of the merits of the question, but he could not help feeling that the way in which these arsenical organic compounds behaved in pernicious anæmia was closely analogous to their behaviour in diseases occasioned by protozoa—he meant especially trypanosomes. If one injected animals suffering from nagana with salvarsan, for a time they seemed to be cured; the parasites disappeared

from the peripheral circulation, and the animals gained in weight. But there was always a relapse, and further injections kept the disease at bay for a shorter period; and eventually there came a time when the salvarsan no longer had any effect on the parasite.

Dr. F. PARKES WEBER: Amongst the non-syphilitic diseases in the treatment of which salvarsan and neo-salvarsan have been employed, an important place must be given to diseases of the blood and blood-forming tissues. Dr. Byrom Braunwell has already dealt specially with pernicious anæmia. F. Perussia<sup>1</sup> claims a remarkably good result in a grave case of splenic anæmia. The patient was a woman, aged 30, whose general condition was thought to be too bad to justify the operation of splenectomy. Three intravenous injections of salvarsan, each of 0.3 grm., were given. The improvement which followed was so rapid that Perussia asks himself whether it was due to a general effect of arsenic on the blood-forming tissues of the body, or whether it should be regarded as a specific effect of the salvarsan on as yet unknown micro-organisms which cause the disease. There was apparently no evidence whatever of syphilis in Perussia's case, and the blood serum gave a negative Wassermann's reaction, but it should be remembered that congenital or acquired syphilis may undoubtedly sometimes play a part in producing the clinical picture of splenic anæmia (in adults) or "Banti's disease."

In the following case of splenic anæmia treatment by neo-salvarsan constituted only part of the arsenical therapy employed, but the result was very good.<sup>2</sup>

The patient, Mrs. S. A., a pale, dark-skinned Turkish woman, aged 30, was admitted under my care at the German Hospital on October 16, 1912, with chronic enlargement of the spleen and a leucopenic type of anæmia. The spleen felt hard and extended downwards to the anterior superior iliac spine and across the middle line, three finger-breadths to the right of the umbilicus. The liver was apparently not enlarged. The conjunctivæ had a very slightly subicteric tinge. The urine was of rather high colour, free from bilirubin, but giving a positive reaction for urobilin and urobilinogen. The fæces were well coloured. The patient was said to have been healthy as a child, and up to the time of her marriage (six years ago). Five years ago (after her first confine-

<sup>1</sup> F. Perussia, *Münch. med. Wochenschr.*, 1912, lix, p. 1482. See also abstracts bearing on the subject in *Folia Hematologica*, Leipz. (Zentral-Organ), 1912, xiii, p. 176, and 1913, xiv, pp. 185 *et seq.*

<sup>2</sup> I showed the patient at the Medical Society of London on January 27, 1913.—F. P. W.

ment) she suffered from "rheumatic fever." She had an abortion (in the second month) three and a half years ago. During the two last years before admission she had suffered from lassitude, and during the last year her menstrual loss had become scanty. Under treatment (with occasional interruptions) by arsenic—namely, by Fowler's solution, arsacetin, and finally by intravenous injections of neo-salvarsan—the spleen decidedly diminished in size, the anæmia vanished, the patient gained in body-weight, the menstrual flow increased, and there was a subjective sense of improvement. At the end of January, 1913, the spleen reached only to the middle line and downwards to about the umbilical level. The patient's weight, which was about 7 st. 7 lb. on admission, was then 8 st. 10½ lb. The conjunctivæ had lost their previously yellowish tinge and the urine no longer gave the reactions for excess of urobilin and for urobilinogen, which were at first present. The injections of neo-salvarsan were three in number: 0.45 gm. on January 13, 0.3 gm. on January 23, and 0.45 gm. on February 8.

Blood examination (Dr. Bauch) on October 21, 1912: Hæmoglobin, 35 per cent.; red cells, 3,300,000 to the cubic millimetre of blood; white cells, 1,500. On November 22, 1912: Hæmoglobin, 45 per cent.; red cells, 3,480,000; white cells, 3,950 (of which—lymphocytes, 38.6 per cent.; polymorphonuclear neutrophiles, 52.7 per cent.; monocytes, 4.6 per cent.; eosinophiles, 1.8 per cent.; myelocytes, 2.3 per cent.). On January 7, 1913: Hæmoglobin, 55 per cent.; red cells, 3,880,000; white cells, 6,000 (of which—lymphocytes, 41.2 per cent.; polymorphonuclear neutrophiles, 42.8 per cent.; monocytes, 9.2 per cent.; eosinophiles, 6.8 per cent.). On January 27, 1913: Hæmoglobin, 65 per cent.; red cells, 5,960,000; white cells, 4,250 (of which—lymphocytes, 60.2 per cent.; polymorphonuclear neutrophiles, 36.5 per cent.; monocytes, 2.2 per cent.; eosinophiles, 1.1 per cent.; no mast cells). The red cells (in stained blood films), which at first showed anisocytosis, polychromatophilia, and moderate poikilocytosis, appeared normal when examined on January 27. In the stained blood films no nucleated red cells were ever seen, except on October 28, 1912, when one normoblast was noted. There was (January 27) perhaps very slightly increased fragility of the red blood cells as tested by graduated hypotonic saline solutions, partial hæmolysis occurring with 0.45 per cent. and complete hæmolysis with 0.4 per cent. aqueous solutions of sodium chloride. The blood plasma (January 27) was of normal yellow colour, transparent, and apparently free from bilirubin. A negative Wassermann's reaction for syphilis was obtained with the patient's blood serum (Lister Institute, October, 1912). On February 11 the

red cells numbered 5,400,000 to the cubic millimetre of blood, and the white cells 4,600; hæmoglobin, 75 per cent. The red cells seemed quite normal. On March 13, when I last saw the patient, she looked very well, and the spleen, which seemed not to be very hard, could be felt reaching only two or three finger-breadths below the costal margin.

It is probable that this case would likewise have done well with other arsenical preparations had not neo-salvarsan been given.

I have not yet used salvarsan or neo-salvarsan in leukæmia, but my colleague Dr. Karl Fürth, at the German Hospital, has given neo-salvarsan in a typical case of chronic myeloid leukæmia (the old "spleno-medullary leucocythæmia"), which I have often seen, and to which he has kindly allowed me to refer. The case was that of a man, aged 50, of fairly strong build and only moderately anæmic, but with a count of 364,000 white cells (chiefly polymorphonuclear leucocytes, myelocytes, and myeloblasts) to the cubic millimetre of blood. Two small intra-venous injections of neo-salvarsan (0.15 and 0.3 grm. respectively) were followed by considerable febrile reaction, and the blood condition was rather worse than better afterwards. Other methods of treatment were therefore adopted.

I have as yet had no opportunity of trying salvarsan or neo-salvarsan in a typical case of Hodgkin's disease (lymphoma granulomatosum), but I should very much distrust any rapid results obtained. The disease, notably in adults, usually begins by a decidedly local enlargement of lymphatic glands, the glands on one side of the neck and near the clavicle constituting the group most frequently involved. Under treatment, especially by X-rays and ordinary arsenical preparations, the mass of enlarged glands may rapidly subside, but this apparently good result is often followed by rapid enlargement of intra-abdominal lymphatic glands and by involvement of the spleen and liver, and then by pyrexia, increasing cachexia, and death. In genuine cases of Hodgkin's disease (notably in adults) early local subsidence of the glandular swelling in the neck does not warrant a favourable prognosis. I refer especially to this because salvarsan is already beginning to be tried in Hodgkin's disease, and because I believe that early diminution of a superficial glandular tumour is a pitfall for error in regard to prognosis.

I have given salvarsan (or neo-salvarsan) in two cases of malaria with resistant crescent forms of parasites in the blood. The first patient was a German sailor, aged 24, admitted to the hospital in November, 1911, with fever and ordinary intra-corpuscular forms of malarial parasites in his blood. When quinine was given the fever promptly ceased, but extracellular crescent-shaped parasites (which had apparently previously



escaped notice) were observed free in his blood. The ordinary intra-corpuseular forms had vanished. I then gave him an intravenous injection of original salvarsan (0.4 gm.), but two days later the crescent forms were still present in his blood (Dr. G. Dorner). Unfortunately, the patient, as he had no fever and felt well, insisted on leaving the hospital and I lost sight of him. The second patient was a German ship's stoker, aged 25, who in October, 1912, was admitted to the hospital with fever of the tertian type and some enlargement of the spleen. Many of his red blood cells contained characteristic ordinary intra-corpuseular plasmodia, but there were likewise some free crescent forms present. Quinine treatment promptly removed the fever. I then (October 19) gave him an intravenous injection of neo-salvarsan (0.6 gm.) and ordered the quinine to be discontinued. Nine days afterwards (October 28), the temperature suddenly rose to 105° F., with shivering, and one or two malarial parasites of the small "signet-ring" type were discovered in the red corpuscles. Two days later, October 30, during a rigor, with fever up to 105.2° F., examination of the blood (Dr. Bauch) showed a great many parasites of similar (small "signet-ring") type. On the following day I injected (intravenously) 0.45 gm. neo-salvarsan, but on the next day (November 1) there was again a rigor and the temperature reached 104.4° F. Shortly after the rigor the blood was examined and plasmodia of the small "signet-ring" type were again found in the red corpuscles. Two days later (November 3) there was again a rigor, with fever up to 104.6° F. Evidently, therefore, the neo-salvarsan employed had not succeeded, like the quinine had, in checking these "tertian" pyrexial symptoms. Half a gramme of sulphate of quinine was then ordered twice daily and soon checked the fever, which did not return as long as the patient remained under my observation. He left the hospital not very long afterwards (November 14) and the blood was not further examined, but it is obvious that in this case the neo-salvarsan (in the doses employed) had much less effect on the febrile manifestations of the disease than the quinine had.

Salvarsan has apparently been found occasionally useful in troublesome cases of chorea minor,<sup>1</sup> including one case of chorea gravidarum,<sup>2</sup>

<sup>1</sup> See E. Mayerhofer, *Wien. klin. Wochenschr.*, 1911, xxiv, p. 976; J. Salinger, *Münch. med. Wochenschr.*, 1912, lix, p. 1376; L. Szametz, *ibid.*, p. 2333. Weill, Mouriquand, and Goyet (*Ann. de méd. et de Chirurg. enfant, Par.*, 1912, xvi, p. 720) claim a good result from rectal injections of salvarsan in severe chorea.

<sup>2</sup> Haertel, Gynäkologische Gesellschaft in Breslau, February 27, 1912, *Monatschr. f. Geb. u. Gyn.*, 1912, xxxv, p. 634.



and it would be interesting to know if it exercised any favourable action in acute rheumatism; it has, I think, been tried in some cases, but in ordinary acute rheumatism the progress under modern treatment is sufficiently satisfactory to make one hesitate to resort to new methods.

Salvarsan has been employed with benefit in cases of Vincent's sore throat and also in noma.<sup>1</sup> At present I have under my care at the hospital a young man, aged 18, who was admitted with stomatitis and developed a severe inflammatory infiltration of the right cheek. There is extreme anæmia, and there has so far been a leucopenia rather than a leucocytosis, but he seems to be improving under small intravenous injections of salvarsan.<sup>2</sup>

Salvarsan has likewise been tried in scarlet fever and other acute febrile infections, and F. Klemperer and H. Woita<sup>3</sup> think that it exercises some genuine specific action in scarlet fever.

In one typical advanced case of disseminated sclerosis, with a negative Wassermann's reaction for syphilis, I tried, in 1911, an intravenous injection of original salvarsan (0.4 grm.), but apparently without any benefit to the patient, though no disagreeable reaction followed the injection, not even a rise of temperature.

In rebellious cases of chronic lichen planus, and in some cases of pemphigus, it is probable that salvarsan will prove itself useful in the future, but sufficient trials in such cases seem not yet to have been published. In the case of a man, aged 31, who had been subject to urticaria and "giant urticaria" for five years, I last year gave two intravenous injections of original salvarsan (each of 0.2 grm.) and one of neo-salvarsan (0.6 grm.). Afterwards he was temporarily free from urticaria and giant urticaria for some time, but that freedom has, unfortunately, not lasted.

Salvarsan and neo-salvarsan have undoubtedly been fairly often tried in cases of malignant diseases (sarcoma and carcinoma), but few results have been published, and probably the results obtained have not been particularly encouraging.

<sup>1</sup> M. Nicoll, jun. (*Arch. of Pediatr.*, New York, 1911, xxviii, p. 912), records the case of a boy, aged 5, successfully treated with salvarsan (two intravenous injections, each of 0.3 grm.) for noma, after the onset of severe scarlet fever. In Vincent's sore throat local applications of salvarsan solutions have been recommended by some.

<sup>2</sup> The improvement did not continue. Examination of the blood showed hardly any hæmopoietic reaction, and death occurred on May 5, 1913. The necropsy proved the case to be one of so-called "aplastic" anæmia.

<sup>3</sup> Klemperer and Woita, 29 *Deutsch. Kongress f. inn. Med.*, April, 1912, *Deutsch. med. Wochenschr.*, 1912, xxxviii, p. 921.

Dr. WILLIAM HUNTER said he had had but slight experience with salvarsan or neo-salvarsan in pernicious anæmia; indeed, his experience with it was restricted to two cases, one of which would be shown to the meeting. The chief reason of his limited acquaintance with the drug was that he had been able to get such good results by other measures of treatment. He would first draw attention to one or two points in the natural history of the disease, which were appropriate to the Section. It was known to be a very grave and severe disease, and those who had seen such cases for a long time knew how difficult, in the early days, it was to procure even moderate improvement in such cases, and especially to get a continuance of that improvement. He wished now to make the statement that there was no form of anæmia which had such remarkable powers of recovery as had pernicious anæmia; the suddenness of recovery of a patient from the condition he could only speak of as startling. He had had patients lying unconscious, with the blood reduced 20 per cent., yet with an improvement in a week to 50 or 60 per cent., and looking very much improved. It was encouraging during treatment to have in mind this tendency for the recovery to be remarkably rapid. There was a remarkable compensatory power (with hyperplastic changes) in the bone-marrow in this grave disease (as in the specimen he now showed). He also showed a specimen of pure white bone-marrow, which was associated with that grave form of anæmia which he had separated out under the name "septic anæmia"; it was the plastic, non-compensatory type of anæmia which was associated with chronic sepsis. He had notes of about 150 consecutive cases of pernicious anæmia, all presenting the features mentioned by Dr. Bramwell during the last fifteen years. He was particularly interested in Case XII, for there had been an opportunity of post-mortem examination. Two and a half years ago that man was brought to him (Dr. Hunter) when he arrived from South Africa. During the two months that he was under care the 20 per cent. was increased to 60 or 70 per cent., and he returned to South Africa. This was now the fourth year since he was first seen, and Dr. Bramwell said he had, when he saw him, a fairly good blood count. He (Dr. Hunter) had now cases going on three, four, five and more years, and one he still had under care which had recovered for thirteen years. The better results he was having were due to the antiseptic treatment which he had adopted during the last ten or twelve years. A patient came to him thirteen years ago, and the 22 per cent. was increased to 65 per cent. in six weeks; that occurred under antiseptic treatment and the use of

antistreptococcic serum. He went out with 80 per cent. quite well. A year later he came back and was down to 60 per cent. Improvement quickly occurred, and he went up to 90 per cent. Five months later he came again, looking rosy and well, but he had beginnings of anæmia, with gastric symptoms and lemon colour. Improvement rapidly occurred, and he remained well until his third year. In that year he had a serious relapse, and came down to 30 per cent. After treatment he went up to 80 or 90 per cent. again, and next visit he went up to 85 to 100 per cent., at which latter figure he had remained for the last seven years. Such prolonged recovery was connected, in his experience, with most stringent antiseptic measures. His previous experience had been that it was difficult to get improvement beyond 60 or 65 per cent. It was his practice to hold the arsenic back at the moment he was sure recovery was taking place, and in that way he had something in hand to fall back upon. He had never used the large doses recommended by some. The first case for which he had used salvarsan had made no appreciable improvement. The second case was under his care now, and the remedy—salvarsan—had been used on him at another hospital. The man was now in the second year of his disease and was extremely ill all last year. He was admitted into Dr. Hunter's wards last December. The first case to whom he referred was given neo-salvarsan, 0·2, 0·4, 0·6, 0·8, last September and October. He got a little better and went out. But he quickly relapsed, and since this last admission he had had nothing but the usual antiseptic measures, with small doses of liquor arsenicalis by the mouth. In the treatment of pernicious anæmia he attributed most importance to antiseptic measures, combined with the use of arsenic. For five weeks his temperature was 102° and 103° F., and the blood value was down to 14 per cent., and the red corpuscles to 20 per cent. The leucocytes were 2,300. The temperature began to fall, but in the fourth week it was still irregular. The chart (exhibited) showed both pulse and temperature still falling. The man said he was now feeling better than he had felt for a long time. His corpuscles were, however, only 34 per cent. and the hæmoglobin 50 per cent. He was not making much blood, but his disease was arrested for the time being.

He showed a man with the disease who came a year ago; he had had the disease three or four years, and a year ago he had slight peripheral nerve symptoms. He had made a recovery from 34 to 70 to 80 per cent. in six weeks. He was away twelve months, and now came with

symptoms of combined sclerosis. His blood now showed 60 per cent. and hæmoglobin 80 per cent., and it might be said to be in a condition of relative stability. He showed the glossitis which he had described as the most characteristic feature in the disease.

The profession was greatly indebted to Dr. Byrom Bramwell for having made and recorded this valuable series of observations with salvarsan. Still, his own experience had been that such results were now common as the result of strict antisepsis alone, and he had not felt it necessary to use the latter drug as its use was always attended with certain grave risks.

Mr. J. E. R. McDONAGH: Prior to the discovery of salvarsan, with the exception of some of the earlier synthetic arsenical compounds which paved the way thereto, our treatment of diseases with drugs was very largely empirical. No sooner had salvarsan been used and its wonderful therapeutic effects had been noised abroad, than the medical profession at large, knowing little of Ehrlich's chemo-therapeutic work, and being so accustomed to empiricism, had that defect so strongly stimulated that they saw in salvarsan the cure for all; with the result that it has already been employed in nearly every disease known. Ehrlich discovered that arsenic when synthetically prepared in an organic compound could be rendered non-toxic except to protozoa, and therefore that its administration would kill the parasites without in any way injuring the host. Salvarsan was made with the idea, then, of being an anti-protozoal drug, and experience has taught us that it is only a specific for diseases caused by that group of organisms. The protozoal diseases with which we are most familiar are yaws, recurrent fever, syphilis, malaria, and sleeping sickness. I have named them in the order in which they are most markedly benefited by the drug under discussion.

Yaws and recurrent fever need only be alluded to in passing, as neither disease is found in this country. In the Dutch West Indies and elsewhere, where there were special hospitals for yaws, since the advent of salvarsan they have been able to be closed. In certain districts in Russia where the mortality from recurrent fever was as high as 5 per cent., it has since been reduced to *nil*.

If malaria could be caught before the parasite had entered the sporulation stage and treated with salvarsan, no doubt every case would be cured, but unfortunately the organism has gone through several phases, as in syphilis, before the disease is attacked, with the result

that certain phases which can exist in the resting stage remain uninfluenced by a series of injections and are capable of giving rise to recurrences later, by starting the cycle again. In malaria salvarsan may cut short an attack, it may cause the disappearance of a recurrence, and it may even very considerably lengthen the period between the recurrences (judged by the regular recurrences which patients were prone to have before being put under treatment), but it cannot be said to cure the disease. On most cases of the tertian form salvarsan exercises a beneficial effect, which is often reversely the case on both the tropical and quartan types. Many cases of malaria become quinine-resistant, as cases of syphilis may to mercury, and in both instances this resistance can be broken down by a course of salvarsan, with the result that the first recurrence after salvarsan can be made to disappear at once with quinine, in the case of malaria, and with mercury in that of syphilis, when prior to the salvarsan treatment these respective drugs proved unavailing. A resistance to salvarsan can also be acquired by protozoa, and that is why its use in sleeping sickness has been so disappointing, because in most of the cases in which it has been tried the patient has had previous treatment with the earlier organic synthetic compounds of arsenic; nevertheless, it can be said that trypanosomes vanish from the blood quicker, and remain absent over a longer period after salvarsan than after any other drug. The tendency in all protozoal diseases is no doubt to ultimate recovery, and in some few cases of malaria, syphilis and sleeping sickness recovery no doubt takes place without any treatment; and although salvarsan has been proved to have a direct destructive action upon the protozoa themselves, I am more inclined to the view that its action is rather to enhance that inherent tendency which the host possesses towards spontaneous cure. In my opinion, this is also the mode of action of vaccines.

Vincent's angina, which is caused by a spirochæte living in symbiosis with what is regarded as a bacillus, disappears at once after salvarsan. Protozoal diseases have a point in common in that they give a positive Wassermann's reaction. Therefore I propose now to consider that group of diseases in which a positive Wassermann's reaction may be obtained, but in which the cause has not been proved to be a protozoon. This group includes scarlet fever and the tubercular form of leprosy. Concerning the former, reports are increasing which testify to the beneficial effect of salvarsan provided the injection is given in the earliest stage of the disease. As regards the latter, I can only say that I have injected three cases, without noticing in any the slightest improvement.

The next group I propose to take is one which comprises diseases which are varied in nature but common, in that arsenic is generally prescribed for them. Let us begin with psoriasis and lichen planus. On several occasions I have treated both conditions with salvarsan, but only with very marked benefit in one case of acute generalized lichen planus; the improvement I noticed in the other cases could have been equally well obtained with arsacetin, orsudan, or soamin. This has also been my experience with the various forms of leukæmia. Although there has been clinical improvement in some of my cases it was only temporary, and the patient soon relapsed into his old condition, and during no stage of the improvement did a differential blood count show any change. This has also been the case with pseudo-leukæmia cutis and mycosis fungoides, but some cases of sarcoma cutis have been reported as being cured. Another skin disease for which arsenic is invariably prescribed is pemphigus vegetans; some cases of this disease have been reported as being benefited, while others have remained uninfluenced.

The next group I will consider contains diseases the cause of which is uncertain, and in which salvarsan has been extensively tried. Small-pox, according to Marks, behaves like scarlet fever provided the patient is put under treatment in the initial stages of the disease. If given before the rash is too pronounced it will stop it from getting worse, and the patient recovers without complications. If prescribed when the rash is at its height the drug has no influence whatever on the future course of the disease. In several cases of disseminated sclerosis salvarsan has been tried, but I am unaware of a single case in which there has been even the slightest improvement. Amongst my cases of syphilis I have had one man who was a martyr to hay-fever. He had suffered from hay-fever thirteen years before he contracted syphilis, and the symptoms began invariably on May 30 for the last fifteen years. The attack was ushered in with the usual symptoms, fever, and the patient was practically blind for forty-eight hours. The hay-fever continued throughout June and July and then disappeared as quickly as it began. During the time it lasted the patient would get frequent bouts of swelling of the eyes, nose and lips, so that he would be obliged to spend days at a time in a dark room. The patient received treatment from me first in November, 1911. As Wassermann's reaction was positive, in May, 1912, I advised patient to have some more salvarsan. On May 24, 1912, the patient began his treatment of five injections. When he received his first injection he stated that he felt that his hay-fever was coming on, and his eyes were very injected and painful.



Within forty-eight hours of the first dose every one of his hay-fever symptoms disappeared and the patient was entirely free throughout that summer.

The last group to be considered contains diseases with a bad prognosis, in which salvarsan had been given as a last resource—namely, malignant disease. Although Professor Czerny has written from time to time upon the good effects he has obtained in non-operative cases of cancer, I can say, with my very limited experience, that the only condition which I have seen benefited at all was carcinoma of the tongue. This is not surprising considering that the great majority of cases of cancer of the tongue occur on a syphilitic basis, and it is the chronic active syphilitic glossitis that improves, not the epithelioma. The improvement may be maintained for a few months, so that every case of epithelioma of the tongue which supervenes on a syphilitic glossitis should certainly be given salvarsan, and every case of syphilitic glossitis with suspicious swellings and fissures should be given salvarsan before an operation is advised. I have had under my care six patients who had been advised to lose their tongue for a wrongly diagnosed epithelioma, who have been so far improved that it would now be difficult to ascertain where the suspicious lesion was situated.

In many cases of malignant disease, and especially in sarcoma, where in late cases the fear from hæmorrhage is great, death may be precipitated from this cause owing to the great vaso-dilating effect that salvarsan often exercises in diseased areas, and this explains the cause of deaths from hæmatemesis which have occurred after salvarsan had been prescribed in patients who were suffering from gastric ulcer.

Some French observers have recently stated that salvarsan will help cases of polyarticular gonococcal arthritis; this is certainly not my experience, and I have never seen a case of gonococcal infection or a soft sore, or its complication, the *ulcus molle serpiginosum*, in the very slightest degree influenced by salvarsan. This also applies to tubercular affections and to the *granuloma tropicum*, a condition probably caused by a capsulated bacillus resembling that found in *rhinoscleroma*, and probably identical with the *pneumobacillus*.

From the above you will notice that salvarsan is a specific for protozoal diseases and may even be used as a test for determining the same. Salvarsan, according to reports, appears to be able to check the progress of diseases which, as far as our insufficient knowledge allows us to judge, we consider to be caused by the group of ultramicroscopic



organisms which are provisionally ranked as protozoa. Therefore, it might be wise to try salvarsan in early cases of anterior poliomyelitis, measles, and mumps.

In no bacterial disease does salvarsan appear to be of any use, and in those diseases of unknown origin in which arsenic is employed with benefit, little more will be derived from the administration of salvarsan than from that of orsudan, soamin, or even increasing doses of Fowler's solution.

Dr. ALEXANDER MORISON said he proposed to speak on the same lines as Dr. Byrom Bramwell had done. His first information on the employment of salvarsan for pernicious anæmia came from Dr. Bramwell at a meeting of the Society of Physicians in Glasgow in March, 1912. It happened when he returned to London that he had a case of pernicious anæmia in his wards, the patient being a man, aged 58. He was admitted on April 1, and remained in the hospital until July, 1912. When admitted to the ward he had well-marked symptoms; his total reds were 1,331,000, whites 6,000, colour index 1·2, and he had poikilocytosis. He was given four injections intramuscularly of salvarsan at intervals of a week, each equivalent to 2 gr. of arsenic, and he improved very rapidly. When he left in July he had hæmoglobin 80 per cent., the reds had risen to nearly 3 million, and his colour index was 1·5. He resumed a light occupation. But, as such cases are apt to do, he returned, on the last day of December, in much the same condition as when he first presented himself. On this occasion, instead of giving him large doses of salvarsan, he gave him a dose equal to  $\frac{1}{2}$  gr. of arsenic, increasing to 1 gr., and he had altogether six intramuscular injections. The poikilocytosis disappeared, the reds increased to 3,200,000, the colour index was 1·2, and he had now been away from the hospital for some time. Possibly the case would relapse. Dr. Parkes Weber had referred to Hodgkin's disease, and it happened that when the case just referred to was in hospital he had also a boy, aged 15, the subject of Hodgkin's disease. He had a moderate temperature. When admitted his hæmoglobin was 50 per cent., reds  $3\frac{1}{2}$  million, whites 19,000, and he had marked symptoms of Hodgkin's disease, glands enlarged in neck, groin, &c. He had injections equal to 2 gr. intramuscularly. His hæmoglobin percentage rose to 70, his total reds to 4 million, and his whites to 50,000. After a time this latter figure fell to 42,000. Though he remained in hospital some time, he did not think his condition was materially altered.

He wished also to refer to the case of a young woman who had only recently been admitted to hospital. She was said to have been running a temperature for three weeks, having been in failing health for altogether eighteen months. She was extremely anæmic, in fact her total reds were only 800,000, whites 7,800, and her hæmoglobin 50 per cent. She had swollen legs and face, flaccid heart, with bruits at the apex, a pulmonary base, &c. The spleen and liver could be felt, and were both tender. There was no poikilocytosis, but she had nucleated red cells (normoblasts) and one megaloblast was seen in the field. She had occasional attacks of epistaxis, and one occurred while she was in hospital. Her menstruation was regular. It was an acute case, but had many of the features of pernicious anæmia. Two days after an injection of salvarsan, equal to 1 gr. of arsenic, her reds had increased to 960,000, her whites to 9,800; and on the tenth day her temperature had reached the normal, and the blood, examined on April 11, showed hæmoglobin 50 per cent., red cells 2,800,000. She had another similar dose, and after that lost all the tenderness which she had when she was admitted: her hæmoglobin was now 50 per cent., her reds  $3\frac{1}{2}$  million, and she was and felt in every way very much better. The diagnosis of pernicious anæmia here might be open to some doubt, but the facts he had given showed that she had not a common form of anæmia. It was difficult, when judging of the effect of any drug, to say whether the measures employed were responsible for the results which followed; but those in contact with cases were better able to form an opinion than were those who got the information at second hand. Whatever the ultimate effects of treatment of pernicious anæmia by salvarsan might prove to be, the Section must feel indebted to Dr. Byrom Bramwell for having so clearly related both the successes and the failures in the cases with which he had had to deal. He (the speaker) when having to deal with a case of pernicious anæmia would be definitely inclined, from his experience of the drug, to employ it.

Dr. S. M. COPEMAN, F.R.S., said he was glad to have had the opportunity of being present, because he owed to Dr. Byrom Bramwell a debt of gratitude, seeing that his early work on pernicious anæmia led him (Dr. Copeman) to investigate that disease, and to take part in the considerable amount of physiological and pathological research which had been done on the blood. One or two points in the demonstration, however, were not clear to him. Several of the deaths mentioned by Dr. Bramwell were due to pneumonia, and he had

wondered whether the treatment could have had anything to do with the onset of the pneumonia. The figures given in regard to Case X seemed quite extraordinary; there was a doubling of the number of red corpuscles in about a week, which, of course, would be admitted to be absolutely phenomenal. When participating in the recent discussion held by this Section on the treatment of cancer by other than operative means, he referred to the fact that Dr. Bernstein and he had made use of salvarsan in cases of malignant disease, but in not one of them could an improvement be attributed to the use of the drug. From what Mr. McDonagh had said he could only assume that they were not cases in which there was any underlying strain of syphilis. Two years ago there were threatenings of a small-pox epidemic in London, therefore, having learnt that Haller had recorded certain cases of the disease as having benefited by the drug, he obtained a grant from the Royal Society, intending to make trial of it in the treatment of small-pox. But the investigation was cancelled by the disease disappearing. It occurred to him, however, that it could be tested in a disease which, some years ago, he had experimentally proved to be specifically related to small-pox—namely, vaccinia. This investigation was carried out by Dr. Bernstein and himself on a considerable number of rabbits at the Brown Institution. The rabbit was capable of being infected with vaccinia, and it was used in the Government lymph laboratories as a routine method of testing and regenerating lymph supplies. But unfortunately the results of using salvarsan in vaccinia were absolutely negative. In some cases the inoculation was made into the marginal vein of one ear, and in others merely on the shaved skin of the back: it was not necessary to make a puncture. They waited various intervals, from six days to a few minutes only, before inoculating with salvarsan; but in no instance was the course of the eruption modified. They noticed a much greater redness of the eruption on the shaved back of the animal after salvarsan had been inoculated, probably on account of the dilatation of the vessels. One point of interest which resulted from these experiments was that the lethal dose of the drug for the rabbit was considerably larger than previously had been realized. In cancer, as in vaccinia, his results with salvarsan had been completely negative.

Dr. GEORGE C. LOW sent the following contribution: Salvarsan has now been used in quite a number of tropical diseases and in those of a spirochaetal nature the results have been quite as satisfactory as in syphilis. It has, perhaps, been most successful in the treatment of

yaws, a disease in some ways resembling syphilis and due to the *Treponema pertenue*, Castellani. First used by Strong in the Philippines, Castellani in Ceylon, and Alston in Trinidad, the use of the drug has now been extended to many of the other Colonies, and reports from them all speak very favourably of it. The drug has been given intramuscularly or intravenously, more so, probably, by the former method than the latter, owing to the ease of administration. Perry, in Ceylon, considers that salvarsan is an effective cure for yaws (parangi), with the possible exception of tertiary cases in which destruction of bone has occurred. He treated fifty-four cases, his dose varying from 0.3 to 0.6 gm., the injection being made intramuscularly or intravenously. Cockin, in Grenada, treated twenty-two cases intramuscularly, and only one case required a second injection, the spirochætes disappearing from the tissues within forty-eight hours. Hughes, in St. Lucia, recommends 0.6 to 0.8 gm. In some of his cases complete cure took place in a little over a week. In one or two a second injection was required. Recurrences had not been noted when he wrote his paper, but sufficient time had not elapsed for him to make a definite statement on this point. Harper, from Fiji, and other writers, are equally enthusiastic about the drug. Summing up our knowledge of the subject, one may say that one dose of salvarsan 0.6 gm. may cure the disease; in a few cases a second or even a third dose is required. Recurrences are rare.

*Relapsing Fever.*—Several cases have now been treated by salvarsan. Koch, for example, has reported two in Hong Kong. The drug was given intravenously in doses of 0.5 and 0.6 gm. respectively. In both cases the parasites disappeared from the circulation within six hours and the patients rapidly recovered. The drug causes a rapid disappearance of spirochætes of this type from the blood of experimental animals also.

*Trypanosomiasis.*—The most extensive trial of salvarsan in the treatment of human trypanosomiasis has been made by Brodin, Rodhain and Corin, in the Belgian Congo. They used the drug either alone or in conjunction with trypaflavin, the doses given being 0.4 to 0.6 gm. Their conclusions are that the drug has a rapid and energetic action on *Trypanosoma gambiense*, the parasite of sleeping sickness, and a beneficial action on the patients themselves. If given early enough, they believe complete sterilization of the blood from trypanosomes may take place, the drug acting best in the first stages of the disease, when the cerebrospinal fluid is not changed cytologically. Several of their cases relapsed, however. A case of Rhodesian trypanosomiasis, under

Sir Patrick Manson's care at the Seamen's Hospital, Albert Docks, received two injections of salvarsan. The drug had no apparent effect on the trypanosomes nor on the general condition of the patient. It may be noted, however, that the patient was not in the early stages of the disease, and he had been subjected to previous treatments with atoxyl, antimony, &c. The matter is still *sub judice*.

*Malaria*.—Opinions vary as to the action of salvarsan on the plasmodia of malaria. A fairly extensive trial has now been given it, but it cannot in any way be looked upon as a specific, nor will it displace quinine. In benign forms of the disease, those due to the benign tertian parasite, *Plasmodium vivax*, or to the quartan parasite, *Plasmodium malariae*, a certain amount of success has followed its use, disappearance of the parasites from the peripheral blood, fall of temperature, &c., but it has not been proved as yet to prevent relapses. In malignant forms of the disease due to the *Plasmodium falciparum* the drug is not effective against the attack nor against subsequent relapses.

*Leprosy*.—Wellmann and others have reported cases of leprosy treated by salvarsan. The drug has practically no effect on this disease, or at least no more so than any other arsenical, acting as a general tonic, would have.

*Pellagra*.—Martin, in America, reviews the history of twenty-seven pellagrins who were treated by means of salvarsan. According to him, twenty of these were completely cured, three were doubtful, while four died. He believes the drug has a specific action on this malady. Niles, on the other hand, is by no means so enthusiastic about it, and states that he does not believe the drug does any good.

*Tropical Ulcer*.—This condition would appear to be due to a spirochæte, the *Spirochæta schaudinni*. Such being the case, one would expect satisfactory results from the use of salvarsan, and reports to hand indicate that this is so.

*Ulcerating Granuloma*.—The drug has also been tried in this condition.

*Kala-azar*.—So far as I am aware no reports of salvarsan in the treatment of kala-azar have yet been published. Considering the nature and zoological affinities of the parasite it is not likely that the remedy will benefit the condition materially.

*Filariasis*.—Some cases have been reported, but whether any good accrued from the treatment cannot be definitely stated. On the whole, it is unlikely that the adult worms lying in the lymphatics will be affected, and if they are not, then the cure is useless.

Dr. BYROM BRAMWELL, in reply, said he had simply brought his experience and laid it before the Society, and he wished to thank the Section for the way in which it had received his remarks. It had been a great satisfaction to him to hear that he had done anything to stimulate Dr. Copeman in his work. Of his deaths, only two were from pneumonia. One died of croupous pneumonia some time after the administration of salvarsan, and he thought the pneumonia should not be debited to the treatment. The death from broncho-pneumonia might have had some connexion with the salvarsan; he would not go further than that. He had listened with great interest to Dr. Hunter's remarks, but he was afraid that his results were not equal to Dr. Hunter's in pernicious anæmia. Dr. Hunter had brought valuable evidence in support of the view that pernicious anæmia was probably due to a toxin absorbed from the intestine acting on the blood in the portal circulation, and that the bone-marrow lesion was secondary to that; but he (Dr. Bramwell) was not convinced that this was the whole truth. He thought it not unlikely that if the disease were due to a toxin, that toxin might act on the bone-marrow as well as on the blood, and that the lesion in the bone-marrow might not be altogether a secondary reparative change. And that led to the further supposition that if the bone-marrow was at fault, as Pepper long ago supposed, it was, perhaps, primarily a weakness of the bone-marrow, to which some destruction of red corpuscles was superadded. But one was so far working in the dark as to the exact causation of pernicious anæmia that all these therapeutic observations were practical rather than scientific. The results must be taken for what they were worth, without supposing that they went to the root of the matter. Salvarsan probably acted in cases of pernicious anæmia by strengthening the red cells, and if that was so, the results one might expect were only palliative. After hearing what Dr. Hunter said, he would in future direct his attention more to oral sepsis than he had done, though he had always considered the condition of the mouth, and had any defective teeth attended to. He did not, however, attach the same importance to oral sepsis as did Dr. Hunter; he had seen so many cases in which either there were no teeth, or in which the teeth were quite sound. He regarded the glossitis as a symptom of the disease, not a cause. He had tried salvarsan also in other diseases, such as Hodgkin's disease, leukæmia, and malaria, but his experience with it in those cases was too small to deserve any weight; therefore, he had abstained from mentioning that part of his experience.

## **Therapeutical and Pharmacological Section.**

May 20, 1913.

Professor W. E. DIXON, F.R.S., President of the Section, in  
the Chair.

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### **Results obtained with Sensitized Vaccine in a Series of Cases of Acute Bacterial Infection.**

By M. H. GORDON, M.D.

FOR the specific treatment of cases suffering from an acute bacterial infection two chief methods are at present in use: either an immune serum containing antibodies specific for the infecting micro-organism is given, or an attempt is made to stimulate the patient's system to the active production of antibody by giving him a vaccine of the infecting micro-organism.

From the practical standpoint, each of these methods has its advantages, and both have shortcomings. Apart from the possibility of giving rise to anaphylactic shock, or serum sickness, immune sera, with the exception of diphtheria antitoxin and one or two others, have over and over again proved disappointing clinically. Ordinary vaccines, again, have the disadvantage, that before the period of increased immunity which they evoke is reached the patient has to pass through a phase during which his resistance is actually lowered. While it is true that this negative phase may in many cases be minimized, and rendered invisible clinically, by using a small initial dose, by increasing the dose slowly, and by properly interspacing the doses, the risk is nevertheless a real one; and those who have had much experience of vaccine treatment—especially in acute cases—must occasionally have seen instances



in which, owing to the specific hypersensitiveness of the patient, this diminution of resistance has proved a serious matter.

The law discovered by Ehrlich and Morgenroth, that every cell when brought in contact with its antibody fixes this antibody to the exclusion of all else, rendered it possible for Besredka to introduce a method of immunizing that promised to form a step forward. This method is as follows: By the simple process of bringing the vaccine into contact with homologous immune serum the bacterial cells attract to themselves their specific antibodies present in the serum, and become coated therewith. After sufficient time has elapsed for the absorption of antibody to take place the bacterial cells are centrifuged out, the supernatant serum is removed and replaced by saline, the deposited bacteria are shaken up and again centrifuged out. Thus all traces of serum may be removed, and a deposit is obtained which consists entirely of bacterial cells coated with their specific antibodies. This is the sensitized vaccine of Besredka.

There are one or two practical points that may be mentioned. It is advisable to count the vaccine before bringing it into contact with the immune serum. It is convenient to carry out all the stages in a graduated centrifuge tube. The vaccine is best killed after sensitization, and this may be done by adding a suitable antiseptic to the saline with which the terminal washing is effected. Besredka appears to be in favour of not killing the vaccine at all, but of giving sensitized vaccine alive. Broughton Alcock has given living sensitized typhoid bacilli, streptococci, and staphylococci to patients without reaction. This measure, however, implies great confidence in the sensitizing properties of the sera used. Personally I have hitherto preferred to use sensitized vaccines in which the bacteria have been killed by phenol; but I have given living sensitized streptococci to two cases of ulcerative endocarditis without harmful effect.

The question now arises, what is the advantage of sensitizing a vaccine? Surely a vaccine treated with immune serum in this way is neutralized, and rendered inert?

The answer to these questions is furnished by the results of the numerous experiments on animals that have been made by various independent observers since 1902, when Besredka introduced the method. These experiments show that the first great effect of sensitization is to reduce the toxicity of a vaccine.

*Examples.*—The plague bacillus retains a good deal of its pathogenicity even when killed by heat. Thus  $\frac{1}{10}$  to  $\frac{1}{15}$  c.c. of a forty-eight

hours' agar culture of plague killed by heat produces a fatal effect on a mouse in forty-eight hours. After sensitization two whole heated agar cultures (twenty to thirty times the previous dose) can be injected into a mouse without producing any symptoms at all. The dysentery bacillus is also very toxic, even when killed. After sensitization, however, one hundred times the dose previously fatal may be given to mice without harmful effect.

These experiments, and others to which I have alluded elsewhere, demonstrate the pronounced effect of sensitization in reducing the toxicity of a vaccine.

The question may next be asked: But is not this reduction of toxicity effected at the expense of the immunizing capacity of the vaccine? The animal experiments show that this is not so. Experiments with the typhoid bacillus, plague, cholera, dysentery, streptococcus, and pneumococcus indicate that the immunity resulting from sensitized vaccine is as "solid" as that resulting from an ordinary vaccine. They show, moreover, that sensitization has the very important effect of accelerating the onset of the immunity, and further, that between the time of injection of a sensitized vaccine and the onset of the resulting immunity there is no diminution in the animal's resistance.

From these experiments on animals, then, it would appear that sensitization of a vaccine has three important advantages—e.g.: (1) The reaction is eliminated; (2) immunity is accelerated; (3) this immunity is achieved without any diminution in the animal's specific resistance.

*How are these Results to be Accounted for?*—The commoner pathogenic bacteria—e.g., streptococci, pneumococci, *Bacillus coli*, *Bacillus typhosus*, *Bacillus tuberculosis*, &c., all act by reason of their endotoxin. During sensitization the bacterial bodies become coated over with agglutinin and opsonin. The endotoxin is not neutralized—at any rate not completely—but merely covered over. When a sensitized vaccine is injected into the body these prepared bacteria, thanks to their opsonification, are at once taken up by the body cells and especially by the polymorphonuclear leucocytes. The endotoxin is not set free until the bacterial cell is lysed in the interior of the phagocytes; and these phagocytes being the chief factory of antibodies, their interior is the very place which we wish to stimulate in a bacterial infection. Thus the object in sensitizing a vaccine is to promote its phagocytosis, and the effect of sensitization is to accelerate immunity by shortening the preliminary work of the phagocytes and causing them to deal at once

with the endotoxin of the invading bacteria. This view, which corresponds with that already put forward by Broughton Alcock, seems to be the most likely explanation of the mode of action of sensitized vaccine. Whatever the *modus operandi*, there is no doubt about the resulting immunity, and the advantage of the method of Besredka is that this is achieved without a reaction, without any trouble from horse serum, speedily, and without producing any diminution in the animal's specific resistance.

The chief experimental work with sensitized vaccines has been done for purposes of prophylaxis. Experiments as to their curative value are less abundant. A striking piece of research, however, in this sense has been carried out by Levy and Aoki, with the pneumococcus on rabbits. They first of all compared the immunizing values of ordinary and sensitized pneumococcal vaccine prophylactically, and found that the sensitized vaccine gave best results. They also found that exceedingly good immunity resulted from vaccinating by the intensive method of Fornet and Müller, according to which increasing doses of vaccine are given for three days in succession. Finally, they injected rabbits with a fatal dose of living pneumococci, and found that they could save the lives of these animals by giving them large enough doses of sensitized pneumococci killed by phenol.

In view of these encouraging results on animals, it was clearly desirable to ascertain the value of sensitized vaccines on man, especially in the treatment of acute bacterial infections. Through the cordial co-operation of the clinical staff at St. Bartholomew's Hospital it has been possible to do this in a series of cases which I am now, through their courtesy, permitted to report.

Before dealing with the results I will ask you to consider for a moment the nature of the problem. We are dealing with a patient whose infection is in active progress, and whose general condition is sufficiently serious to justify admission to hospital. Some of the cases of which I shall show the temperature charts were, in fact, so exceedingly ill at the stage when the treatment was applied that there was grave doubt as to their recovery.

The first question is, what would a sensitized vaccine be expected to do in such a case? Now the method being one of stimulating the patient's specific resistance, it is clear, before we start, that the main factor in a patient's recovery from an acute bacterial infection must always be his own general resistance. All that we can hope to do with a method such as the present one is to bring out his specific resistance

to the utmost extent possible, and in the speediest time; in short, to *accelerate* the immunizing mechanism of the patient. I think you will agree that if we are able to do this without detriment to the patient in other respects, we have a therapeutic measure that in certain cases is likely to prove of very valuable service indeed.

The second question which I wish to raise is this: How are we to judge of the effect of a sensitized vaccine on such a patient? There can be only one answer. The effect will be seen by comparing the clinical condition of the patient—both local and general—before and after the vaccine is given.

I am showing the temperature charts of these cases. But the temperature is, of course, only one point in the illness. In some cases the general condition of the patient, his facial appearance, his comfort, appetite, capacity for sleeping, and general subjective feeling, as also the appearance of the local lesion, may be profoundly altered for the better without the same degree of improvement showing in the temperature chart. Bearing this in mind, however, it must be admitted that in an acute bacterial infection the temperature forms on the average as good and impartial an index of the patient's general condition as any other single point can do.

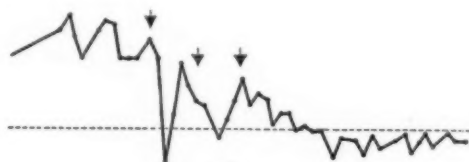
All of the cases received the ordinary non-specific treatment. The great majority were instances of infection by *Streptococcus pyogenes*. They were injected with stock sensitized *Streptococcus pyogenes* vaccine made by mixing three or five strains of typical *Streptococcus pyogenes* and sensitizing them. The vaccine was killed after sensitization by adding 1 per cent. of phenol. In giving the vaccine the intensive method of Fernet and Müller was chiefly used, increasing doses being injected subcutaneously for three days in succession.

#### NOTES ON CASES.

*Case I.*—N. N., a little girl, aged 10, was admitted under the care of Sir Anthony Bowlby on account of an attack of erysipelas of the face and scalp. On the third day of her illness the erysipelas was spreading both forward and backwards, and the patient was slightly delirious. At 10 p.m. aspirin was given by mouth, and 100 million sensitized *Streptococcus pyogenes* vaccine subcutaneously. Twenty-four hours later the swelling had extended somewhat further, but the margins were less defined than before. The temperature was a little lower, but the patient was still delirious. Five hundred millions of vaccine were given. On the following morning the

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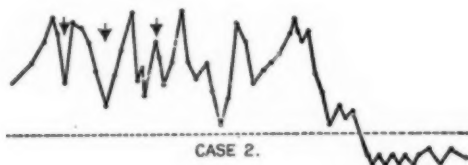
patient was very much better, the area had not spread, the margin was far less defined, the œdema had diminished, and her temperature had fallen to 98°2' F. The evening note of the same day read as follows: "This is the first evening since admission that the child has not been delirious. The local condition is also much improved." One thousand million sensitized streptococci were given. She continued to improve, and three days later the child was quite well.



CASE I.

The arrows show when the sensitized vaccine was given.

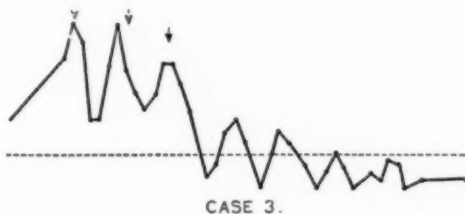
*Case II.*—E. J., a nurse, was admitted under the care of Sir Anthony Bowlby on the fifth day of an attack of cellulitis of the scalp, accompanied by cervical adenitis, the result of scratching the scalp with a comb. On admission the patient's temperature was 101° F., pulse 120, respiration 24. Bacteriological examination of fluid taken from below a crust that had formed



CASE 2.

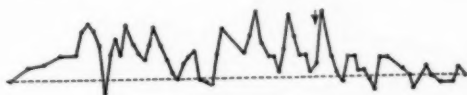
at the point where the scalp had been scratched showed *Streptococcus pyogenes* to be present as well as *Staphylococcus aureus*. Thereupon the patient was given 100 million sensitized *Streptococcus pyogenes* vaccine. On the following day the patient's condition had not improved, the local œdema had spread, and a blood culture was made with 5 c.c. of the patient's blood, which, however, failed to show growth. Five hundred million of the vaccine were given, followed twenty-four hours later by 1,000 million. Besides the vaccine treatment, the local œdematous region, which showed some fluctuation, was incised, and later some suppurating glands in the left occipital region had to be opened. The vaccine appeared to produce no effect on either the local or general condition of this patient, and forty-eight hours after the third dose the front of the scalp, which had previously been only swollen and œdematous, became erysipelatous. Two days later, however, the erysipelas subsided, the temperature fell, and she began to convalesce.

*Case III.*—Nurse S. was admitted under the care of Mr. D'Arcy Power suffering from an attack of erysipelas of the forehead and cheeks. On admission her temperature was  $104^{\circ}$  F., pulse 120, respiration 24. Coincidentally with the administration of three successive doses of 100, 500, and 1,000 millions of sensitized *Streptococcus pyogenes* vaccine at twenty-four-hourly intervals the inflammation proceeded to subside and the patient to get well.



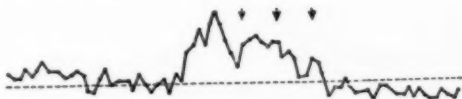
CASE 3.

*Case IV.*—J. K., aged 24, a strong, healthy housebreaker's labourer, was admitted under the care of Mr. Bruce Clarke for a compound fracture of the lower end of the left humerus sustained by falling down 15 ft. through



CASE 4.

a concrete floor which he was breaking up. The fracture suppurated and the patient developed some pyrexia. Cultures from the wound showing *Streptococcus pyogenes*, the patient was given a single dose of 100 million sensitized *Streptococcus pyogenes* vaccine. Thereupon the local condition improved and the pyrexia rapidly subsided.

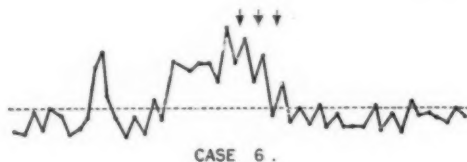


CASE 5.

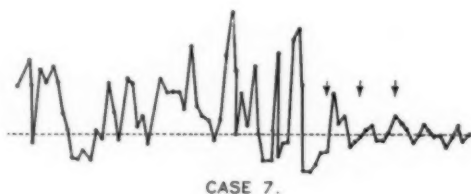
*Case V.*—A. H., male, aged 31, under the care of Sir Anthony Bowlby, had Symes's amputation performed on his left foot for extensive tuberculous disease there. In spite of every care the stump began to suppurate, and *Streptococcus pyogenes* being found present, the patient was given increasing doses of sensitized *Streptococcus pyogenes* vaccine on successive days. The local improvement was very marked in this case. The patient's general condition improved correspondingly, the temperature reaching normal within eight hours of the third injection.

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*Case VI.*—G. C., a young medical man, was admitted under the care of Mr. Harmer, under the following circumstances: The patient had for some time past suffered from his tonsils, which were septic, and enucleation was accordingly performed. The patient did badly and developed double otitis media and left mastoiditis. In spite of further operation his condition became exceedingly grave, extensive suppuration having developed in the mastoid region and in the subcutaneous tissue around. *Streptococcus pyogenes* being found present in the pus, the patient was given 50 c.c. of anti-*Streptococcus pyogenes* serum (B. W. and Co.). On the following day the patient was no better. After consultation with Mr. Harmer we decided to try sensitized *Streptococcus pyogenes* vaccine. The patient was given 50 million, and on the following days 100 and 500 million. The improvement, both locally and generally, was rapid and



well marked; the pain and suppuration became diminished and the temperature "stepped down" after each dose until it became normal.

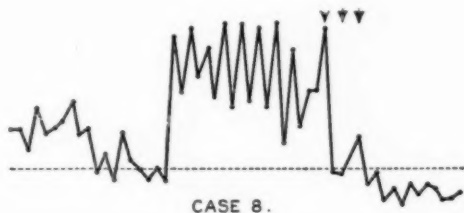


*Case VII.*—M. M., a boy, aged 8, was admitted under the care of Mr. C. Ernest West with a temperature of  $103^{\circ}4'$  F., pulse 108, respiration 30, and delirious. There was a thick, yellow, offensive discharge from the left ear. During the night the patient vomited three times. On the following day a radical mastoid operation was performed by Mr. West who found and drained an extradural abscess. The lateral sinus was exposed but not opened. On lumbar puncture the cerebrospinal fluid was found to be under increased pressure, but clear, and in other respects normal; and when lumbar puncture was repeated on two occasions later the fluid was also found normal. The pyrexia continuing, the lateral sinus was packed off and opened, but no clot was found. On the following day, the patient having had a rigor and a temperature of  $107^{\circ}4'$  F., the lateral sinus was explored but no pus was seen, nor was any found on exploring the brain. The pyrexia continuing and a blood culture



having yielded *Streptococcus pyogenes*, the patient was given 50 million sensitized *Streptococcus pyogenes* vaccine, followed on the succeeding days by 100 and 500 million. The chart shows the effect upon the temperature. The note on the day after the third dose says: "The patient is better and the temperature is steadying down." A week later the patient was able to get up for his dressing. Six days later a flap was cut and the wound closed over. The child made an uninterrupted recovery.

*Case VIII.*—E. M., aged 28, housewife, was admitted under the care of Mr. D'Arcy Power suffering from abscesses in both breasts and pyrexia. The mastitis had come on ten days after confinement and had been present for over a fortnight. The abscesses were treated by incision and free drainage, but in spite of this the temperature kept up and the patient's general condition did not improve. The question of endocarditis arose, and Dr. Herringham was called in, whose report was as follows: "There is a faint systolic murmur. No friction (pericarditis). No discoverable affection of the lungs. Abdomen



CASE 8.

appears natural. It is possible that she has septic endocarditis, but it is not like the usual onset, and there is nothing in the sounds of the heart that proves its existence." Thereupon a blood culture was made and yielded *Streptococcus pyogenes* in pure culture. The patient was then given 100 millions of sensitized *Streptococcus pyogenes* vaccine, followed at twenty-four-hourly intervals by 500 and 1,000 million. The temperature fell after the first dose from 104° F. to subnormal, and the local condition showed a marked improvement. The note states that "the patient feels much more comfortable and takes more interest in her surroundings." Another blood culture was then made and proved negative. The patient continued to improve, and a month later was discharged cured, a faint systolic murmur being still audible at the apex.

*Case IX.*—S. S., a woman, aged 64, was admitted under the care of Mr. Bruce Clarke, suffering from an advanced stage of streptococcal septicaemia and with thrombosis of the left internal saphenous vein. As she was evidently suffering from septicaemia on admission, and the strong probability was that the infecting micro-organism was *Streptococcus pyogenes*, and the sensitized vaccine could do no harm even if the patient were infected by

another micro-organism, she was given a dose of 250 millions of sensitized *Streptococcus pyogenes* vaccine straightway, and then the internal saphenous vein was ligatured in the upper third of the thigh and about 4 in. of varicose vein filled with clot dissected out and removed. The patient slept well during the night, but next morning was still delirious and her pulse was intermittent. Cultures made at the operation from the patient's blood, taken from the median basilic vein and also from the clot removed from the internal saphenous vein showed a large number of colonies of *Streptococcus pyogenes*. The patient was given 500 and 1,000 million sensitized *Streptococcus pyogenes* vaccine, but without any effect, and she died on the second day after admission. At the post-mortem examination, in addition to the streptococcal septicæmia, endocarditis was found present, vegetations being present on aortic cusps.

*Case X.*—J. C., aged 71, under the care of Sir Anthony Bowlby, had a large carbuncle, 5 in. in diameter, at the back of his neck. At first the patient improved under treatment, but later his illness took a turn for the worse. He was examined bacteriologically and found to be suffering from infection with *Streptococcus pyogenes*. Sensitized vaccine was applied in the usual way, but without any effect. At the post-mortem examination the heart weighed 21 oz., and the mitral ring was completely calcified. The patient was also found to have streptococcal meningitis.

*Case XI.*—A housewife, aged 28, was admitted under the care of Sir Francis Champneys, two days after delivery, suffering from laceration of the vaginal wall and streptococcal endometritis. The uterus was empty. She was given an intra-uterine douche, and three doses of sensitized vaccine at twenty-four-hourly intervals. The sequence of events was as follows:—

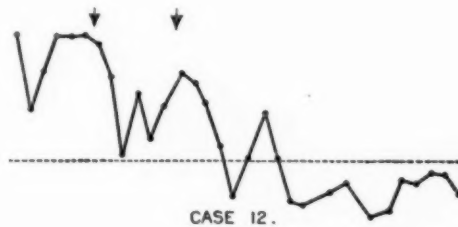
| Date        |     | Vaccine     |     | Temperature |     | Pulse |
|-------------|-----|-------------|-----|-------------|-----|-------|
| December 16 | ... | 100 million | ... | 102° F.     | ... | 114   |
| " 17        | ... | 500 "       | ... | 101.5° F.   | ... | 106   |
| " 18        | ... | 1,000 "     | ... | 100.5° F.   | ... | 88    |
| " 19        | ... | —           | ... | 99.4° F.    | ... | 96    |

The patient's temperature rose to 103° F. on December 20 and 21, but then subsided, and she made an uneventful recovery.

*Case XII.*—S. C., housewife, aged 33, was admitted under the care of Sir Francis Champneys, having been delivered two days previously of a still-born child. On admission the patient was somewhat cyanosed, the temperature was 102° F., and the pulse 120. The uterus was empty, but gave a growth of *Streptococcus pyogenes*. She was given doses of 100 and 600 million sensitized *Streptococcus pyogenes* vaccine on two successive days. The temperature subsided and she got well. (See chart, p. 163.)

*Case XIII.*—D. P., aged 20, was admitted under the care of Sir Francis Champneys, nine days after confinement. The uterus was found to contain

pieces of retained blood-clot and placenta, which were removed. The endometrium gave a pure culture of *Streptococcus pyogenes*, but a blood culture was negative. The uterine cavity was swabbed with 12 c.c. of anti-pyogenes serum and the same amount of serum was also given subcutaneously. Subsequently she was given a lysol douche night and morning. The patient was given three doses of sensitized *Streptococcus pyogenes* vaccine in the usual way, but although her general condition apart from the temperature appeared to improve, her pyrexia did not disappear until ten days later. After that she made an uninterrupted recovery.



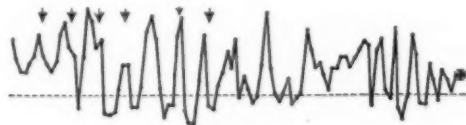
Case XIV.—E. R., aged 39, had a miscarriage fourteen days before admission under the care of Sir Francis Champneys, and her temperature had been raised for a week. On admission the temperature was 101'6° F., pulse 112, cervix movable, canal closed, some discharge, uterus not enlarged, ante-flexed, and freely movable. A blood culture gave a pure culture of *Streptococcus pyogenes*. The patient was given two doses of sensitized *Streptococcus pyogenes* vaccine in the usual way. Her temperature subsided and general condition improved. A further dose of 1,000 million was given some days later for prophylactic purposes. She made an uninterrupted recovery.

Case XV.—A. F., aged 25, was admitted under the care of Sir Francis Champneys, seven days after delivery. Her confinement had occurred in the absence of a doctor, and she had suffered from continual pain and headache since. On admission her temperature was 104° F., pulse 120, respiration 32, uterus bulky and fixed on one side. Internal os closed. The uterus was evacuated, blood-clot and membrane being removed. Cultures from the uterus gave *Streptococcus pyogenes*, but the blood culture was negative. Two days later she developed signs of pleurisy at the right base, her blood culture became positive, and she showed signs of free fluid in the abdominal cavity. Doses of sensitized streptococcus vaccine were applied, beginning on the second day after admission, but the patient failed to respond. Towards the end, when the patient's condition was desperate and she had to be infused with saline, 500 million sensitized streptococcus vaccine were put into the saline and

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given intravenously, but with no effect. She died on the thirteenth day after admission. Permission for a post-mortem examination could not be obtained.

*Case XVI.*—A. H., aged 36, admitted under the care of Sir Francis Champneys, had an apparently normal confinement a week before admission. Two days after delivery, however, she felt ill, shivered, and developed a profuse discharge. On admission on the fifth day of her illness the uterus was found to be 3 in. above the pubes and tender. The perineum was lacerated, the cervical canal was patent and showed a copious discharge. On further examination the uterine cavity, though large, was found to be empty. Cultures were made from the uterus and blood, and the uterine cavity was swabbed out with iodine. The uterine culture gave a growth of *Streptococcus pyogenes* and the blood culture remained sterile. The patient was given sensitized *Streptococcus pyogenes* vaccine in doses of 100, 500, and 1,000 million on three successive days, but failed to improve. She developed signs of consolidation at the left base and the abdomen became distended, and 2,000 millions of the vaccine were given, but without effect. The patient got progressively worse. A needle was put into her left chest, and some pus withdrawn which showed *Streptococcus pyogenes* in pure culture. The blood also gave a growth of the same micro-organism at this stage. The patient's condition becoming desperate, she was given 1,000 million sensitized streptococcus vaccine intravenously, but without effect, and she died on the seventh day after admission. At the post-mortem examination, besides the streptococcal septicæmia she was found to have a double empyema and also a pint of purulent fluid in the peritoneal cavity. Both fluids showed *Streptococcus pyogenes* in pure culture. The endometrium was found to be sloughing.

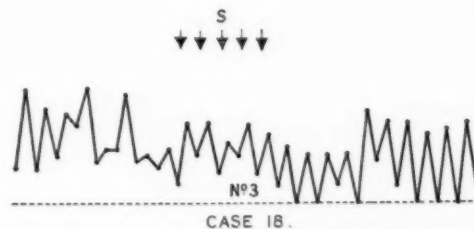
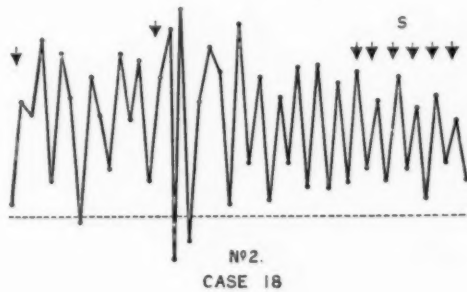
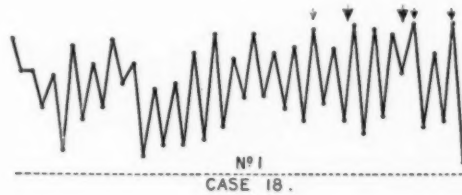


CASE 17.

*Case XVII.*—E. F., admitted under the care of Sir Francis Champneys, had aborted four days before admission, when the placenta and membranes were also expelled. On admission the patient's blood gave a copious growth of *Streptococcus pyogenes*, while the endometrium only grew one colony of a staphylococcus. She was given sensitized *Streptococcus pyogenes* vaccine daily, and as she did not respond to smaller amounts the dose was pushed up to 5,000 million. The vaccine, however, was without effect and she died seventeen days after admission. After death, besides the streptococcal septicæmia she was found to have infarcts in the lung and spleen, purulent peri-

tonitis, and also an empyema. The pus in both the latter situations showed *Streptococcus pyogenes* in pure culture.

Case XVIII.—The next case was that of an undergraduate, aged 21, under the care of Dr. Haynes, of Cambridge, whose note is as follows: "Seen on



The arrows marked S show when sensitized vaccine was given.

evening of February 15, 1913, complaining of 'strained wrist,' which had been painful for two days, but patient had continued to row. On examination some swelling present on the dorsum of the right hand and forearm. Joint apparently not involved; sore on buttocks and base of coccyx. Suppurating blister on left third toe; no glandular swelling. Fomentations applied. Next day condition not changed; no œdema or localizing signs; no recent blisters or abrasions of hand. Patient seemed ill: temperature slightly raised, pulse 80.

A surgeon called in advised arm-bath; no glands enlarged. February 18: Patient removed to nursing home; no improvement; temperature and pulse-rate rising; swelling of arm more marked, but not spreading upwards. February 19: Arm incised above wrist and over dorsum of hand; no pus found. February 21: Incisions enlarged; a little very thick pus from upper wound; culture—*Staphylococcus aureus*; pain over upper third left fibula. February 23: Incision down to fibula, periosteum stripped by pus from upper third. March 7: Incision over lower third left fibula, which was bare of periosteum. March 9: Profuse hæmorrhage (1 pint) from wound in right forearm. March 24: Signs of pleurisy, left. March 26:  $1\frac{1}{2}$  pints clear fluid with flakes of lymph in it, aspirated from left pleura.

"Remarks: This has been a very severe case of septicæmia. The primary infection was probably through the sore on the coccyx, with secondary periostitis of right ulna and radius, metacarpals and carpals, left fibula, and infection of the left pleura. There have been the usual signs of toxæmia, profuse sweatings, delirium, wasting, and profound anæmia. The heart muscle has shown signs of failing."

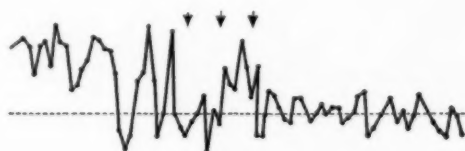
Dr. Haynes grew a *Staphylococcus aureus* from the first pus obtained, and a pathologist later grew a streptococcus. The pleural effusion gave pure *Streptococcus pyogenes*. The specific treatment consisted first of stock staphylococcus vaccine followed by antistaphylococcal serum, of which two doses each of 25 c.c. were given. Autogenous streptococcal vaccine was next tried in doses of 5 million, 6 million, and two doses of 7 million. Polyvalent antistreptococcal serum was also given in three doses of 25 c.c. None of these specific measures appeared to benefit the patient, and in the sixth week, four days after aspiration of the pleural cavity, autogenous sensitized streptococcus vaccine was given daily in doses of 25, 50, 100, 250, 500, and 1,000 million, at the suggestion of Dr. Horder, who had been called into consultation by Dr. Haynes. This was followed later by further doses of 100, 500, 1,000, 1,500, and 3,000 millions of stock sensitized *Streptococcus pyogenes* vaccine.

Dr. Haynes's note of the result is as follows: "Considerable improvement, both local and general, in the condition of patient has occurred since treatment by sensitized vaccine was commenced. The most noticeable events have been: reduction of temperature, cessation to a great extent of delirium, marked increase in appetite, improvement in colour, and more healthy appearance of wounds. During the last few days the temperature has kept a higher average, and the appetite is failing."

*Case XIX.*—This case was that of a lady, aged 62, under the care of Dr. Chittenden Bridges. The original condition for which she came under treatment was a septic throat with enlarged glands on the left side of the neck. These broke down, and were opened by Mr. Cosens Bailey. A few days later she developed erysipelas on the left side of the neck, which gradually spread over the whole scalp, accompanied by a high temperature and rapid pulse. An

autogenous vaccine prepared from pus examined at the time of operation was injected with no benefit. Thirty cubic centimetres of antistreptococcus serum were injected, with no result. Mr. McDonagh having suggested to Dr. Bridges that he should try sensitized vaccine, I was requested by Dr. Bridges to send him some doses of stock sensitized *Streptococcus pyogenes* vaccine. The effect of this sensitized vaccine on the patient's condition, both local and general, was exceedingly well marked. From being desperately ill the patient proceeded to get well. Dr. Bridges, to whom I am indebted for these particulars and the temperature chart, writes that he is confident that the patient would have died had it not been for the sensitized vaccine.

*Case XX.*—L. C., aged 23, under the care of Sir Francis Champneys, was delivered of twins thirteen days before admission. One child was putrid, the other died after a few days. The patient was admitted with bronchitis and an offensive vaginal discharge. The uterus was found to be fixed, but empty. A culture from the uterus showed a few colonies of *Bacillus coli*, and some small colonies of what I at first thought to be streptococcus. The patient was given three doses of sensitized *Streptococcus pyogenes* vaccine, but without benefit. She was then given three doses of autogenous sensitized *Bacillus coli* vaccine, also without effect. Examination of the sputum showing swarms of pneumococci, and the small coccus from the uterine culture having by now been identified with pneumococcus, she was given three doses of stock sensitized pneumococcus vaccine. The effect on the patient was exceedingly well marked and she at once began to improve. This effect was far more obvious clinically, than is seen in the temperature chart. She was a weak, anæmic woman, but convalescence though slow, was sure.



CASE 21.

*Case XXI.*—M. P., a girl, aged 21, was admitted under the care of Mr. D'Arcy Power, suffering from severe abdominal pain and vomiting. Laparotomy was performed, but nothing abnormal found. The patient's pain focusing down into the region of the left kidney, where a tender swelling could also be felt, and pus and *Bacillus coli* being present in the urine, left pyelitis was diagnosed. She was given three doses of autogenous *Bacillus coli* sensitized vaccine, with the result that after the third dose a marked improvement in her general condition set in. This is reflected in the temperature chart. The improvement was maintained, and she made an uninterrupted recovery from symptoms, though *Bacillus coli* was still present in the urine on her discharge.



## SUMMARY.

What, then, is the value of this form of specific treatment as judged by its effect on the cases described above?

I think that this question can best be answered by considering the series of cases, nineteen in number, in which the infecting agent was *Streptococcus pyogenes*. In none of these, or in any of the other cases, was there any evidence to show that the sensitized vaccine had a harmful effect. In order to estimate its clinical value I will first of all take the cases in which it had no effect at all. In seven out of the nineteen cases the vaccine produced no apparent change. Of these seven cases five died. Of the fatal five, two were in an advanced stage of septicæmia when the treatment was first applied. After death, one of these was found to show endocarditis, the other meningitis. All of the three remaining fatal cases were instances of puerperal septicæmia; and it may be noted that in all of them the pleura became infected, and in two of them the general peritoneal cavity as well. There remain two cases of apparently localized streptococcal infection that recovered, but appeared to derive no benefit from the sensitized vaccine. So much for the cases in which the treatment was without effect. The remaining twelve cases all showed a great improvement after administration of the vaccine. At least six of these patients were in an extremely serious condition clinically when this form of immunization was begun. In all, the ordinary medical and surgical treatment had failed to cure. Three of them had streptococci in their blood-stream. The sensitized vaccine was given, the general and local condition improved, the temperature descended, and the patient began to get well. In three of these cases antistreptococcus serum had been given, but without effect. In two of them also autogenous ordinary vaccine had been tried, but with no benefit.

As regards infections with bacteria other than *Streptococcus pyogenes*, our results are as yet too few to speak with confidence as to the relative value of the method. I have tried sensitized autogenous vaccine in two cases of ulcerative endocarditis without the slightest effect. Both were advanced cases, however, one showing 80 and the other 300 to 400 colonies of *Streptococcus salivarius* per cubic centimetre of their blood.

As regards infections by the pneumococcus, again my results are as yet too few for drawing conclusions. Dr. Hamill has made up quantities

of sensitized pneumococcus vaccines, however, and as he is here will be able to give us his experience. Trial is being made of the method in cases of pneumonia by Dr. Tooth and Dr. Horton-Smith Hartley. Two cases of broncho-pneumonia, due to the pneumococcus in children, appeared to derive benefit; but in some others no effect was seen. Besides the case mentioned (Case XX), two cases of acute pneumococcal bronchitis in middle-aged men rapidly cleared up after administration of three successive doses of stock sensitized pneumococcus vaccine. We must also wait for more material before concluding as to the merits of the treatment with *Bacillus coli* infections. The results so far have been encouraging. It has been applied in several severe cases of opened appendix abscess (that threatened to develop general peritonitis) with certainly no harm, and apparently with good localizing effect; but this effect is difficult to prove from the temperature chart, which has simply remained at the normal level after the operation.

I have been disappointed in the use of sensitized staphylococcus vaccine, as I have been unable hitherto to obtain a serum that properly sensitizes the *Staphylococcus pyogenes*. No doubt this difficulty will be overcome.

I have endeavoured to make a trial of sensitized tubercle bacilli (S.B.E.) but the preparation on the market which I made use of had evidently become desensitized, and as half the minimal dose recommended produced somewhat of a reaction, I did not proceed with it.

#### CONCLUSION.

The method of Besredka has the conspicuous merit of producing immunity in animals rapidly, without discomfort, and without producing any preliminary diminution of resistance.

The experience here described with cases suffering from acute bacterial infection goes to show that where there is latent power available in the general resistance of the patient, the method has a similar effect on man under these circumstances. In some instances, moreover, this dormant power of the specific resistance may be awakened by sensitized vaccine even at a comparatively late stage in the attack. In cases in which the treatment did no good there was no evidence to show that it did the slightest harm.

The method should have a great future prophylactically in the face of epidemics. It seems possible that sensitized vaccine may also be

useful prophylactically in hospitals—e.g., by this means the resistance of the patient might be raised to *Bacillus coli*, *Streptococcus pyogenes*, or the pneumococcus before operations on the alimentary tract or other infected area. Similarly, the method is open to the physician for the purpose of preventing secondary infections. Further, a prophylactic dose of sensitized vaccine might be given in cases of difficult labour.

Finally, I submit that in cases already infected, the evidence here brought forward goes to show that in a proportion of instances it is possible by this method to materially promote the patient's recovery. By administering a sensitized vaccine to these patients we appear to bring into action available reserves in that complex and still incompletely defined entity, the patient's specific resistance.

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#### DISCUSSION.

Dr. H. H. DALE was sure there would be a general agreement that Dr. Gordon had been able at any rate to strengthen the case for investigation of this promising line of research and treatment. He wished to ask the author one or two questions. Dr. Gordon said that sensitized vaccines did not keep well—i.e., in time the antibody disappeared and the vaccine became desensitized. Could any idea be given of the degree of permanence? Was it a matter of days, of weeks, or of months? Again, he did not think the source of the serum used was mentioned in the paper. Was it from an immunized rabbit or was it horse serum? Also, had Dr. Gordon any particular method of estimating the potency of the serum before using it in sensitizing the vaccines, so as to assure himself that the serum used would be efficient in sensitizing? He understood Dr. Gordon to say there was a strong reason for assuming that antibodies were formed chiefly by the leucocytes; and he would be glad to hear that elaborated a little, and the evidence on which it was based stated. The last point on which he sought information was as to the rationale of the trouble one took to free these

organisms so completely from the serum, seeing that the serum was said to be good in itself. Why not save all that trouble by simply mixing them and injecting together?

Dr. HAMILL said he had tried the method in regard to other organisms. He had prepared over twenty courses of sensitized pneumococcal vaccine, and these were administered in about ten cases of pneumonia, of which one died. In a disease like pneumonia it was difficult to gather what precisely had been the effect of the vaccine. Many cases when they entered hospital were at about the fourth or fifth day of the illness, and often the history of onset was so vague that one could not accurately gauge the number of days it had existed and hence when the crisis was due. But he derived the general impression that a considerable proportion of the cases so treated had their condition much improved; they took their food and slept better than before the sensitized vaccines were used. He would mention one case in particular. It was that of a child who was desperately ill, with a leucocyte count never above 8,000. After three days' administration of sensitized pneumococcal vaccine the leucocyte count rose rapidly to 20,000 or 30,000, and the child recovered. Another case, of which he exhibited the chart by the epidiascope, was that of an infant, aged 8 months. It was admitted on account of vomiting. The temperature was high, and on admission the weight of the child was 14 lb. 15 oz. It was rather drowsy, and had some rigidity of neck, though not much retraction. Lumbar puncture was performed and blood-stained fluid drawn off. This was repeated four days later, and a profuse growth of meningococcus was obtained; these organisms were also seen in films. Therefore he thought it could do no harm to prepare a sensitized vaccine of meningococcus. One hundred million were given at 3 p.m., and the temperature afterwards rose to 101° F. Next day 250 million were given, and the day after 500 million. The temperature settled down, and the child, from being drowsy soon began to take an interest in its surroundings, and put out its hands eagerly to grasp any bright object brought near it. The temperature went up again, and 250, 500 and 350 million were given on successive occasions. The child improved steadily from that time. After entering the hospital the child's weight decreased to 12 lb. 12 oz., and the increase dated from the use of the sensitized vaccines, the gain being 3½ lb. in the next four weeks. Three months later the child was found to have developed some degree of hydrocephalus. He had not been able to trace the child since the end of March. He had never before seen a child so young recover from so severe an attack of meningococcal meningitis; the temperature chart alone showed that this case was severe. He used the method also in another case of the disease which was in the hospital, and though death ultimately supervened, there had been considerable amelioration of the condition. The age of the child was between 2 and 3 years. After three doses it sat up in bed and took its food well, but it could not be saved.

Dr. LANGDON BROWN considered this to be one of the most important recent advances in therapeutic measures. No one in this country had had so much experience of the method as Dr. Gordon, and most physicians who had employed it had gone to Dr. Gordon for their information. In one case of general pneumococcal infection, he was much struck by the benefit to be derived from pneumococcal sensitized vaccine. A young man had an attack of pneumonia, and there were abundant pneumococci in his sputa. After the crisis he developed an empyema, which was operated on. But he also had very severe general constitutional disturbance, a clot formed in his femoral vein, and his blood culture grew abundant pneumococci. The administration of the first dose of sensitized vaccine coincided with the rise of temperature which was occurring, and it did not prevent it. But after doses on three successive days, in the way recommended by Dr. Gordon, there was a striking improvement and the patient made a good recovery. Though pneumococci could often be obtained from the blood early in pneumonia, the fact that a copious growth could be obtained in this case some days after the crisis showed that the patient was in a serious septicæmic condition, and his rapid improvement with this remedy was impressive. The failures he had had were in cases of *Bacillus coli* infections. One was the case of a woman who had pyelitis due to *Bacillus coli*. She had been treated with ordinary vaccines, but without effect, and the sensitized vaccines had no effect either. The other patient was a man, aged 70, who was admitted on account of rigors. There were no localizing signs. The leucocyte count was only 4,000. Of the acute infections causing leukopenia, *Bacillus coli* seemed to be the most likely, the infection starting from the gall-bladder. *Bacillus coli* was obtained in quantities from the blood, and sensitized vaccines were prepared and used. He did not see the patient after the first dose was given, but the impression of those who did see him was that the treatment made him worse. The man died a few days afterwards; indeed it was the kind of case which one would expect to have that ending, whatever might be done. Cholecystitis and a large spleen were found at the post-mortem. But in the case of pneumococcal septicæmia he did not doubt that the recovery was largely due to the sensitized vaccine.

Dr. R. A. O'BRIEN said his contribution to the debate must take the form of a series of questions. He was much impressed with the recital of Dr. Gordon's cases. The idea of combining passive and active immunization had become fairly prominent of late years. When one, in order to immunize a rabbit or horse, was giving some dangerous toxin, such as diphtheria, or tetanus, it was advantageous to give serum with it in the early stages, as that prevented the overwhelming influence of the toxin and the possible death of the animal. The animal responded to balanced mixtures, toxin and antitoxin, by the production of antitoxin itself later. Some of the most convincing cases of vaccine treatment of streptococcal infection seemed to have possessed the same principle. He referred to a paper published in the *Proceedings*

giving results of the treatment of cases of puerperal sepsis at the London Hospital, at the Rotunda Hospital, Dublin, and at either Edinburgh or Glasgow. Even the sceptic was inclined to admit, in the face of those contributions, that the use of a streptococcal vaccine plus antistreptococcal serum produced an extraordinarily low mortality. With regard to the occurrence of the negative phase, he would like Dr. Gordon to give some of the results of his wide clinical experience. He (the speaker) had thought that the idea of a negative phase, as meaning a lowered resistance or increased susceptibility to disease, was fast disappearing. Typhoid vaccine was used prophylactically, and had often been used in the midst of epidemics, having been given to many nurses in large nursing homes in America and on the Continent, and to garrisons of soldiers where there were many soldiers still liable to infection. The idea that the negative phase was not a real danger was, perhaps, attributable to the use of typhoid vaccine in the treatment of typhoid fever, the doses being given at intervals of two or three days; pneumococcal vaccine was similarly used in pneumonia. If the negative phase which could be demonstrated by laboratory methods, for instance, following the use of vaccines, meant an increased susceptibility on the part of the patient, one would expect typhoid vaccine in typhoid fever to be highly dangerous; experience showed that this was not so. Reference had been made to increased phagocytosis which occurred after the use of sensitized vaccines, and he asked whether it had been observed that sensitized virulent pneumococci or streptococci injected into a patient or animal were phagocytosed more readily than were the non-sensitized organisms. Another point of interest in Dr. Alcock's paper was, that after giving sensitized vaccine the authors could not demonstrate the presence of any kind of ordinary antibodies, nor any complement-binding antibodies; from which fact he concluded that Dr. Alcock considered that the presence of agglutinins and complement-binding antibodies was not a measure of the resistance of the patient. Yet the fact that the vaccine was sensitized was measured by its complement-binding figure. It raised many interesting theoretical considerations, which Dr. Gordon would probably enlarge on in his reply. He would have liked to have heard Dr. Gordon's results in the treatment of chronic cases by this method, but perhaps he would deal with these on a future occasion. He (the speaker) had notes of recent cases treated with antistreptococcal serum prepared from streptococci obtained from the patient's blood in which the disease was infective endocarditis, or at any rate streptococcal septicæmia. The clinicians who used the serum were convinced that the effect was very beneficial. But a sceptical review of the charts was never very convincing; though after some doses there was obviously very marked improvement in the condition of the patient, there were others in which no such result followed. He would be glad to hear whether Dr. Gordon had had experience of long-continued chronic cases, such as where there had been persistent discharge from the ear, or from sinuses, and whether this new method produced good results.



Dr. GORDON, in reply, said that in making up sensitized vaccines it was advisable to use an organism which was virulent. The streptococcus should be taken from the body as quickly as possible, and with as few sub-cultures as possible; one did not wish to run the risk of the virulence being lowered. These vaccines had been kept active for as long as six months; but only after the saline had been drawn off. He had received a warning from Paris that vaccines were liable to become desensitized by keeping. That was more important for them, because in that country they used living organisms, whereas in England dead ones were employed. He (the speaker) would like to try experiments with sensitized tubercle bacilli, but it was such a difficulty that at present he had been unable to do so. The serum which he had used for sensitizing the *Streptococcus pyogenes* had been that of the horse; they had used either the Pasteur Institute serum or the anti-pyogenes serum of Burroughs Wellcome and Co. He believed the former was a little the stronger, because he understood that it was made with living streptococci. With regard to getting rid of the serum, the experiments which had been done on animals showed that the serum interfered to some extent with the immunity. And for that reason, apart from the question of serum sickness or anaphylaxis, he preferred to get rid of the serum. He believed that the serum shortened the duration of the resulting immunity; but he did not definitely know that to be the case in human beings. There was, however, the animal evidence showing that if one did not get rid of the serum the results were not so good as if it was done. The testing of the potency of a serum was a difficult matter. He had used, as a rough index, agglutinin, with a view to making sure that the serum had antibodies specific for the micro-organism which was being sensitized—not as a quantitative, but as a qualitative test. But the real proof of incomplete sensitization was the production of a reaction when the vaccine was given to the patient. He generally gave his sera twelve hours at room temperature in contact with vaccine, and he believed the results were even better by extending the period to forty-eight hours. There appeared to be comparatively little absorption of antibodies from a serum of that kind, because one could find agglutinin present in large quantities after the vaccine had been removed from the serum. With regard to the exact nature of the immunity caused by sensitized vaccine, he thought there was need for a good deal of animal experimentation on this matter. It was being done now in Paris, and he hoped it would also be done elsewhere. The subject would well repay investigation. It was true that Besredka and his colleagues had examined the animals inoculated with sensitized vaccines, and they had not found agglutinin, and although immunity was produced they did not find these particular antibodies. Animal experimentation, however, on the degree and durability of the immunity itself had now been carefully carried out for ten years, and the results were very complete. The only sure test of immunity was the number of fatal doses the treated animal would stand. It was, of course, an expensive process, and meant the sacrifice of many animals. And in that respect the paper of Levy and Aoki came out well. They knew that if they took a certain dilution of



their broth culture of pneumococcus it would kill the animal, and the value of various methods had been tested in this way. One question which he had been asked was as to why he believed that leucocytes were the main factor in producing immunity. His reply was that, so far as he was aware, all the available evidence pointed in that direction. After a leucocytosis had been produced in it, the peritoneal cavity would stand a dose which would otherwise be fatal; and if one took a leucocyte and put it outside the body in saline, in the presence of a suspension of bacteria, though that leucocyte at first could not engulf the organism, and showed no capacity to secrete opsonin, yet if watched for a number of hours it might be seen eventually to do so. That pointed to the leucocyte having the power to manufacture an antibody. He believed leucocytes to be the main factor in resistance because he was not aware of any evidence having been adduced to show that it was not so. He once made an investigation of the distribution of opsonin, and one of the first experiments he did was to kill a rabbit, take serum from all its organs, and also to make extracts of its organs. He endeavoured to make these comparable. He tested the relative opsonin content of the various sera and extracts; and the case in which he got the best phagocytosis was when he used the serum itself of the animal, from whatever organ. The nature of the immunity procured by using sensitized vaccines was not quite certain, but it was almost certainly of the nature of an anti-endotoxin production. And if that were found to be so, then one of the most important factors in immunity would have been laid bare. It was a matter for experimentalists to decide. He felt much interested in what Dr. Langdon Brown said, and especially in the case in which no results were obtained. If a sensitized vaccine made the patient worse, it raised the question as to whether the sensitization had been thorough. Unfortunately, there were not sufficient sera to sensitize all the infecting organisms that were needed. He had sensitized one or two bacteria by immunizing the rabbit against the particular organism in each case. There was no serum available for sensitizing the *Micrococcus catarrhalis*, or the influenza bacillus. No anti-gonococcal serum on the market seemed properly to sensitize the gonococcus. These defects needed supplying, because experience showed that results could be obtained by sensitized vaccines which were not secured otherwise. With regard to the negative phase coinciding with the period of diminished resistance, he was not satisfied on that point, and therefore he preferred to use the term "diminished resistance," rather than "negative phase." He did so because the animal experiments with sensitized vaccines showed that if an animal were given an ordinary vaccine, then for a variable period after it was given the animal could be killed by a smaller dose of the infecting micro-organism than a control animal which had not been touched. That he regarded as very convincing evidence. With reference to the method, if the question of antibodies remained still "in the air," the solid ground of the whole animal test led one to place great reliance upon it. With respect to phagocytosis, it could be shown that by sensitizing a vaccine leucocytes would take up that vaccine far more readily than they would take

up ordinary vaccine. That could be confirmed any day. The opsonin no doubt enabled them to take it up, at least for streptococci ; he was not sure about virulent pneumococci. One of the streptococci he used in his observations he sent to Paris, and they refrained from injecting their horses with it, he understood because it was the most virulent streptococcus culture they had had for years. In Paris the horses were immunized with living streptococci. As regards the exact nature of the immunity, he admitted that there was a point beyond which the information available was as yet incomplete. Whatever the future might have to say as to the theory, certainly the clinical results of the method had been exceedingly good in acute cases, and better than those obtained with ordinary vaccines. A number of chronic cases had also been treated by the method. Mr. Harmer, of the Throat Department of St. Bartholomew's Hospital, had been applying the method to chronic cases, and his results would be placed before the forthcoming International Congress of Medicine.





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